

**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 001-39567**

**C4 Therapeutics, Inc.**

(Exact name of Registrant as specified in its Charter)

**Delaware**  
(State or other jurisdiction of  
incorporation or organization)  
**490 Arsenal Way, Suite 120**  
**Watertown, MA**  
(Address of principal executive offices)

**47-5617627**  
(I.R.S. Employer  
Identification No.)  
**02472**  
(Zip Code)

**Registrant's telephone number, including area code: (617) 231-0700**

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	CCCC	The Nasdaq Global Select 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 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

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant, based on the closing price of the shares of common stock on The NASDAQ Stock Market on June 30, 2022, was \$201,260,869.

The number of shares of Registrant's Common Stock outstanding as of February 15, 2023 was 49,050,851.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement for its 2022 Annual Meeting of Stockholders to be filed pursuant to Regulation 14A within 120 days of the end of the registrant's fiscal year ended December 31, 2022 are incorporated by reference into Part III of this Annual Report on Form 10-K to the extent stated herein.

Auditor Firm ID: 185

Auditor Name: KPMG LLP

Auditor Location: Boston, MA, United States

**Table of Contents**

	<b>Page</b>
<b>PART I</b>	
Item 1. <a href="#">Business</a>	1
Item 1A. <a href="#">Risk Factors</a>	40
Item 1B. <a href="#">Unresolved Staff Comments</a>	83
Item 2. <a href="#">Properties</a>	83
Item 3. <a href="#">Legal Proceedings</a>	83
Item 4. <a href="#">Mine Safety Disclosures</a>	84
<b>PART II</b>	
Item 5. <a href="#">Market for Registrant’s Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities</a>	85
Item 6. <a href="#">[Reserved]</a>	85
Item 7. <a href="#">Management’s Discussion and Analysis of Financial Condition and Results of Operations</a>	85
Item 7A. <a href="#">Quantitative and Qualitative Disclosures About Market Risk</a>	94
Item 8. <a href="#">Financial Statements and Supplementary Data</a>	94
Item 9. <a href="#">Changes in and Disagreements with Accountants on Accounting and Financial Disclosure</a>	94
Item 9A. <a href="#">Controls and Procedures</a>	94
Item 9B. <a href="#">Other Information</a>	95
Item 9C. <a href="#">Disclosure Regarding Foreign Jurisdictions that Prevent Inspections</a>	95
<b>PART III</b>	
Item 10. <a href="#">Directors, Executive Officers and Corporate Governance</a>	96
Item 11. <a href="#">Executive Compensation</a>	96
Item 12. <a href="#">Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters</a>	96
Item 13. <a href="#">Certain Relationships and Related Transactions, and Director Independence</a>	96
Item 14. <a href="#">Principal Accounting Fees and Services</a>	96
<b>PART IV</b>	
Item 15. <a href="#">Exhibits, Financial Statement Schedules</a>	97
Item 16. <a href="#">Form 10-K Summary</a>	99

## SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, or Form 10-K, including the section entitled “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” contains express or implied forward-looking statements that are based on our management’s belief and assumptions, and on information currently available to our management. Although we believe that the expectations reflected in these forward-looking statements are reasonable, these statements relate to future events or our future operational or financial performance, and involve known and unknown risks, uncertainties, and other factors that may cause our actual results, performance, or achievements to be materially different from any future results, performance, or achievements expressed or implied by these forward-looking statements. Forward-looking statements in this Form 10-K may include, but are not limited to, statements about:

- the initiation, timing, progress, results, safety and efficacy, and cost of our research and development programs and our current and future preclinical studies and clinical trials, including statements regarding the timing of initiation and completion of studies or trials, the period during which the results of the trials will become available, and our research and development programs;
- the ultimate impact of the ongoing coronavirus, or COVID-19, pandemic, or any other health epidemic, on our business, manufacturing, clinical trials, research programs, supply chain, regulatory review, healthcare systems or the global economy as a whole;
- risks related to the direct or indirect impact of the ongoing COVID-19 pandemic or any future large-scale adverse health event, such as the scope and duration of the pandemic, government actions and restrictive measures implemented in response, material delays in diagnoses, initiation or continuation of treatment for diseases that may be addressed by our development candidates and investigational medicines, or in patient enrollment in clinical trials, potential clinical trials, regulatory review or supply chain disruptions, and other potential impacts to our business, the effectiveness or timeliness of steps taken by us to mitigate the impact of the pandemic or other future large-scale adverse health event, and our ability to execute business continuity plans to address disruptions caused by the ongoing COVID-19 pandemic or future large-scale adverse health event;
- our ability to obtain funding for our operations necessary to complete further development, manufacturing and commercialization of our product candidates;
- our ability to obtain and maintain regulatory approval for any of our current or future product candidates;
- the period of time over which we anticipate our existing cash and cash equivalents, and marketable securities will be sufficient to fund our operating expenses and capital expenditure requirements;
- our ability to identify and develop product candidates for treatment of additional disease indications;
- the potential attributes and benefits of our product candidates;
- the rate and degree of market acceptance and clinical utility for any product candidates we may develop;
- the pricing and reimbursement of our product candidates, if approved, including the possibility for reduced pricing of our products, once approved, if they are later subject to mandatory price negotiation with the Centers for Medicare and Medicaid Services under the Inflation Reduction Act of 2022 or other applicable laws;
- the effects of competition with respect to any of our current or future product candidates, as well as innovations by current and future competitors in our industry;
- the implementation of our strategic plans for our business, any product candidates we may develop, and our TORPEDO® (Target Oriented Protein Degrader Optimizer) platform;
- the ability and willingness of our third-party strategic collaborators to continue research, development, and manufacturing activities relating to our product candidates, including our ability to advance programs under our existing collaboration agreements with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc., or Roche, Biogen MA, Inc., or Biogen, and Calico Life Sciences LLC, or Calico, or other new collaboration agreements;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates;
- estimates of our future expenses, revenues, capital requirements, and our needs for additional financing;
- future agreements with third parties in connection with the manufacturing and commercialization of our product candidates, if approved;

- the size and growth potential of the markets for our product candidates and our ability to serve those markets;
- our financial performance;
- regulatory developments in the United States and foreign countries;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- the success of competing therapies that are or may become available;
- our ability to attract and retain key scientific or management personnel;
- developments relating to our competitors and our industry; and
- other risks and uncertainties, including those discussed in Part I, Item 1A - Risk Factors in this Form 10-K.

In some cases, forward-looking statements can be identified by terminology such as “will,” “may,” “should,” “could,” “expects,” “intends,” “plans,” “aims,” “anticipates,” “believes,” “estimates,” “predicts,” “potential,” “continue,” or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. These statements are only predictions. You should not place undue reliance on forward-looking statements because they involve known and unknown risks, uncertainties, and other factors, which are, in some cases, beyond our control, and which could materially affect results. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under the section titled “Risk Factors” and elsewhere in this Form 10-K. If one or more of these risks or uncertainties occur, or if our underlying assumptions prove to be incorrect, actual events or results may vary significantly from those expressed or implied by the forward-looking statements. No forward-looking statement is a promise or a guarantee of future performance.

The forward-looking statements in this Form 10-K represent our views as of the date of this Form 10-K. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should therefore not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this Form 10-K.

This Form 10-K may include statistical and other industry and market data that we obtained from industry publications and research, surveys, and studies conducted by third parties. Industry publications and third-party research, surveys, and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. We have not independently verified the information contained in such sources.

## SUMMARY OF RISK FACTORS

Our ability to implement our business strategy is subject to numerous risks that you should be aware of before making an investment decision. These risks are described more fully in Part I, Item 1A - Risk Factors in this Form 10-K. These risks include, among others:

- We are a clinical-stage biopharmaceutical company with a limited operating history and have incurred significant losses since our inception. To date, we have not generated any revenue from product sales. We expect to continue to incur significant expenses and increasing operating losses for at least the next several years and may never achieve or maintain profitability. Our net loss was \$128.2 million and \$83.9 million for the years ended December 31, 2022 and 2021, respectively.
- We will need substantial additional funding to pursue our business objectives and continue our operations. If we are unable to raise capital when needed, we may be required to delay, limit, reduce or terminate our research or product development programs or future commercialization efforts.
- Our approach to the discovery and development of product candidates based on our TORPEDO platform is unproven, which makes it difficult to predict the time, cost and likelihood of successfully developing any products.
- While we are a clinical-stage company and have commenced clinical trials of several product candidates, all of our other product candidates are still in preclinical development. Further, we have never completed a clinical trial of any of our product candidates. Our business could be harmed if we are unable to advance to clinical development, develop, obtain regulatory approval for and/or commercialize our product candidates, or if we experience significant delays in doing any of these things.
- We cannot be certain of the timely completion or outcome of our preclinical testing and clinical trials. In addition, the results of preclinical studies may not be predictive of the results of clinical trials and the results of any early-stage clinical trials we commence may not be predictive of the results of later-stage clinical trials.
- Our preclinical studies and clinical trials may fail to demonstrate adequately the safety and efficacy of any of our product candidates, which would prevent, delay, or require additional research or analysis to proceed with development, regulatory approval, and commercialization of our current and future product candidates.
- We have entered into collaboration agreements with Roche, Biogen, and Calico, and may in the future seek to enter into collaborations with third parties for the development and/or commercialization of certain of our product candidates, but we may never realize the full potential benefits under these existing or potential collaboration arrangements.
- The continuing effects of the ongoing COVID-19 pandemic, including the spread of new strains or variants of the virus and the effects of localized shutdowns, could adversely impact our business, including our preclinical studies and clinical trials.
- We face substantial competition, which may result in others discovering, developing or commercializing products for the same indication and/or patient population before or more successfully than we do.
- We rely, and expect to continue to rely, on third parties for the manufacture of our product candidates for preclinical and clinical testing, as well as for commercial manufacture if any of our product candidates receive marketing approval. This reliance on third parties may increase the risk that we will not have sufficient quantities of our product candidates in a timely manner, or at an acceptable cost or quality.
- If we are unable to obtain required marketing approvals for, commercialize, manufacture, obtain, and maintain patent protection for or gain market acceptance of our product candidates, or if we experience significant delays in doing so, our business will be materially harmed and our ability to generate revenue from product sales will be materially impaired.
- If we are unable to obtain and maintain patent protection for our technology and products or if the scope of the patent protection obtained is not sufficiently broad or enforceable, our competitors could develop and commercialize technology, product candidates, and products similar or identical to ours, and our ability to successfully commercialize our technology, product candidates, and products may be impaired.

**NOTE REGARDING COMPANY REFERENCES**

Unless the context otherwise requires, the terms “C4 Therapeutics,” “the Company,” “we,” “us,” and “our” in this Form 10-K refer to C4 Therapeutics, Inc. and its consolidated subsidiary.

**NOTE REGARDING TRADEMARKS**

We own or have rights to various trademarks, service marks, and trade names that are used in connection with the operation of our business, including our company name, C4 Therapeutics, our logo, the name of our TORPEDO technology platform and the names of our BIDAC and MONODAC protein degrader product candidates. This Form 10-K may also contain trademarks, service marks, and trade names of third parties, which are the property of their respective owners. Our use or display of third parties’ trademarks, service marks, trade names or products in this prospectus is not intended to and does not imply a relationship with, or endorsement or sponsorship by us. Solely for convenience, the trademarks, service marks, and trade names referred to in this prospectus may appear without the ®, <sup>TM</sup> or <sup>SM</sup> symbols, but the omission of such references is not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or the right of the applicable owner of these trademarks, service marks, and trade names.

## PART I

### Item 1. Business.

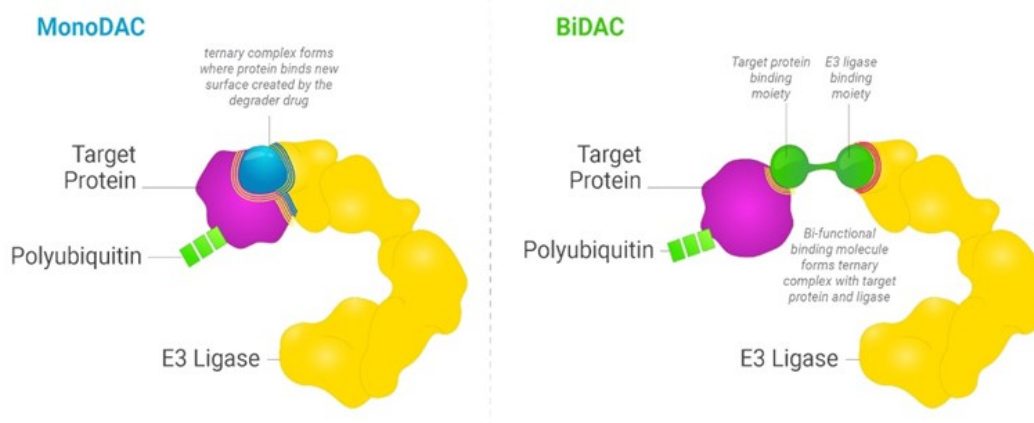
#### Overview

We are a clinical-stage biopharmaceutical company dedicated to advancing targeted protein degradation science to develop a new generation of small-molecule medicines to transform how disease is treated. Historically, the focus in our industry has been on discovering and developing small molecule medicines that inhibit the activity of disease-causing proteins. However, that approach has been limited to only those proteins where chemistry can be used to bind to active sites on the protein and effectively inhibit its activity, which accounts for less than 15% of the human proteome. Furthermore, for those targets where inhibitors have been approved, resistance mechanisms emerge that ultimately render inhibitor approaches ineffective over time. We leverage our proprietary technology platform, which we call TORPEDO, to efficiently design and optimize small-molecule medicines that harness the body's natural protein recycling system to rapidly degrade disease-causing protein, offering the potential to overcome resistance mechanisms, target the 85% of the human proteome deemed undruggable, and improve patient outcomes. We are using our TORPEDO platform to advance multiple targeted oncology programs to the clinic while expanding the platform to deliver the next wave of medicines for difficult-to-treat diseases and ultimately improve treatment options for patients.

Our TORPEDO platform enables the discovery of a new class of targeted investigational small molecule medicines called protein degraders. Protein degraders leverage the body's natural protein disposal system, specifically the ubiquitin-proteasome system, or the UPS, to catalyze the destruction of target proteins. By harnessing the body's natural process for destroying unwanted proteins, targeted protein degradation offers a novel method to treat disease and replicate the benefits of genetic knockdowns with a small molecule approach.

Our degraders enable a family of proteins, called E3 ligases, to come into close enough proximity to disease-causing proteins so that the E3 ligase can "tag" the disease-causing protein for destruction. This is called ubiquitination, which is the process by which an E3 ligase tags a target protein for degradation using a molecular tag called ubiquitin, rather than specific compound-binding sites.

Our TORPEDO platform has the capability to design two types of protein degraders. We refer to the first type of degrader as MonoDACs, which are monofunctional degradation activating compounds and are referred to by some in the industry as "molecular glues." MonoDAC degraders function by binding to E3 ligases and creating a new surface on the E3 ligases that enhances the binding of the E3 ligases to target proteins. We refer to the second type of degrader as BiDAC degraders, which are bifunctional degradation activating compounds. BiDAC degraders are designed so that one end of the molecule binds to the disease-causing target protein and the other end binds to the E3 ligase. This is depicted in the image below.



Each of these degrader approaches is intended to result in the same end point: bringing the E3 ligase in close enough proximity to the disease-causing protein, so that the E3 ligase can "tag" it for destruction.

Our robust chemistry engine and proprietary analytic models of pharmacokinetics, or PK, and pharmacodynamics, or PD, enable us to efficiently design and synthesize degraders for a selected target that are optimized for overall degradation efficiency and properties such as solubility, permeability, and oral bioavailability. These PK/PD models allow us to predict the depth and duration of target degradation *in vivo* and select candidate degraders with confidence.

We have leveraged our TORPEDO platform to develop a robust pipeline reflected in the image below.

Program	Target	Indications	Discovery	Pre-clinical	Early phase development	Late phase development
CFT7455	IKZF1/3	Multiple Myeloma & Non-Hodgkin's Lymphoma				
CFT8634	BRD9	Synovial Sarcoma & SMARCB1-Null Cancers				
CFT1946	BRAF V600	V600 Mutant Cancers				
CFT8919	EGFR L858R	Non-Small Cell Lung Cancer				
Chromatin Regulating Targets		Various Cancers				
Oncogenic Signaling Targets		Various Cancers				
Transcription Factor Targets		Various Cancers				

Our most advanced product candidate, CFT7455, is an orally bioavailable MonoDAC degrader of protein targets called IKZF1 and IKZF3, currently in clinical development for multiple myeloma, or MM, and non-Hodgkin lymphomas, or NHLs. We have selected IKZF1 and IKZF3 as our initial targets because they have a strong mechanistic rationale, a well-defined biology, and targeting them with a novel degrader may address a significant unmet need. In our preclinical studies, CFT7455 has demonstrated potent and selective protein degradation with favorable pharmacological properties. We initiated a first-in-human Phase 1/2 clinical trial for this product candidate in June 2021. In August 2021, the United States Food and Drug Administration, or FDA, granted orphan drug designation to CFT7455 for the treatment of MM. We presented initial clinical data from Arm A at the American Association for Cancer Research Annual Meeting in April 2022. These data showed that single agent CFT7455 resulted in deep and durable degradation of IKZF1/3, as quantified by mass spectrometry, and meaningful decreases in serum free light chain. Neutropenia, a known on-target toxicity associated with IKZF1/3 degraders, was dose-limiting at the 50 µg starting dose on a dosing schedule with a seven-day drug holiday over a 28-day cycle. As a result, the dosing schedule was modified to include a 14-day drug holiday over a 28-day cycle. We continue to enroll patients in the Phase 1 dose escalation portion of the ongoing Phase 1/2 clinical trial at the modified schedule.

Our next most advanced product candidate, CFT8634, is an orally bioavailable BiDAC degrader of a protein target called BRD9, currently in clinical development for synovial sarcoma and SMARCB1-null solid tumors. Historically, BRD9 has been considered an “undruggable” target due to the inability of bromodomain inhibitors to effectively treat cancers dependent on BRD9. Unlike BRD9 inhibition, BRD9 degradation has been shown to be efficacious in preclinical models of synovial sarcoma. In preclinical studies, CFT8634 has shown potent anti-tumor activity in synovial sarcoma cell lines but does not appear to affect normal cells. Further, CFT8634 has shown *in vivo* activity in synovial sarcoma xenograft models when dosed orally. In March 2022, the FDA granted orphan drug designation to CFT8634 for the treatment of soft tissue sarcoma. In May 2022, we initiated the first-in-human Phase 1/2 clinical trial of this product candidate. In January 2023, we shared initial PK and PD data from the initial dose escalation cohorts of the Phase 1/2 trial that demonstrate dose proportional exposure, strong oral bioavailability and deep BRD9 degradation. We continue to enroll patients in the Phase 1 dose escalation portion of the ongoing clinical trial.

We are also developing CFT1946, an orally bioavailable BiDAC degrader specifically to be potent and selective against BRAF V600 mutant targets to treat melanoma, non-small cell lung cancer, or NSCLC, colorectal cancer, or CRC, and other malignancies that harbor this mutation. In preclinical studies, CFT1946 is active *in vivo* and *in vitro* in models with BRAF V600E-driven disease and in models resistant to BRAF inhibitors. In January 2023, we initiated a first-in-human Phase 1/2 clinical trial of CFT1946 for the treatment of BRAF V600 mutant solid tumors including NSCLC, colorectal cancer and melanoma, and continue to enroll patients in the Phase 1 dose escalation portion of the trial.

Additionally, we are developing CFT8919, an orally bioavailable, allosteric, mutant-selective BiDAC degrader of epidermal growth factor receptor, or EGFR, with an L858R mutation in NSCLC. In preclinical studies, CFT8919 demonstrated equipotent activity against EGFR mutations resistant to EGFR inhibition, including L858R-C797S, L858R-T790M, and L858R-T790M-C797S compared to L858R single mutation in Ba/F3 cell models *in vitro*. We completed IND-enabling activities for this program in December 2022.

Beyond these initial product candidates, we are further diversifying our pipeline by developing new degraders against both clinically validated and currently undruggable targets for our own proprietary pipeline and for the pipeline we are developing in collaboration with Roche, Biogen and Calico. We have engineered degraders that have successfully achieved blood-brain barrier penetration in preclinical studies, which is a key step in developing medicines with the potential to treat



brain metastases in oncology, as well as in therapeutic areas such neurodegenerative diseases. We also believe there are many other therapeutic areas and indications where leveraging our TORPEDO platform to develop novel degraders may be advantageous.

In addition to the programs identified above and our early-stage development collaborations with Roche, Biogen, and Calico, we are conducting exploratory research and development work on various other wholly owned assets.

### **Our Strategy**

We are committed to transforming the treatment of cancer and other diseases through the discovery, development, and commercialization of novel therapies that destroy disease-causing proteins.

Key elements of our strategy are to:

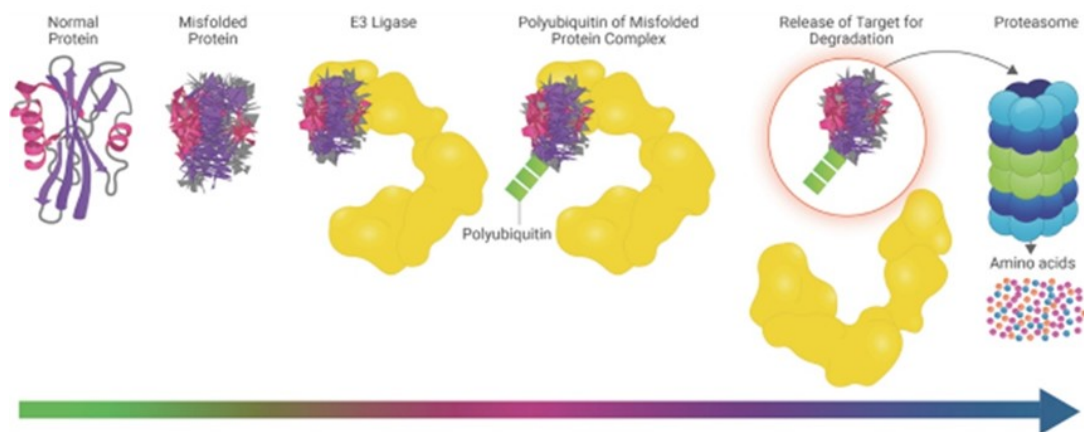
- **Progress multiple small molecule oral oncology degraders in the clinic.** Using our proprietary TORPEDO platform, we have generated novel product candidates for the treatment of cancer, and we believe favorable trial results from our lead programs would offer important validation for both our platform and the future development of those programs themselves. Based on the results of our clinical trials, we will work with the FDA to discuss potential expedited development and accelerated approval pathways for our product candidates as applicable.
- **Advance the next wave of research targets for difficult-to-drug and classically undruggable targets.** We believe we can apply the principles and approaches used to advance our lead programs more broadly to develop novel degraders that have the potential to treat poorly drugged targets or drug currently undruggable targets. Our target selection process focuses on identifying targets where targeted protein degradation could have an outsized patient impact, either by its potential to improve upon existing treatment options or provide new treatments for diseases that currently have no approved therapies. When considering what targets to select, we focus on targets with a clear genetic link to a disease and consider how a degrader is differentiated from an inhibitor or other therapeutic option. Our target selection planning also includes reviewing patient populations and registrational pathways as well as evaluating available biomarker assays to identify which patients may benefit from the investigational therapy. We are focusing our current proprietary programs on selected oncology indications, but we believe our platform has broad applicability beyond cancer that we plan to capitalize on in the future directly or with one or more collaboration partners.
- **Expand the application of the TORPEDO platform through existing and new collaboration partners.** We have existing strategic collaborations with Roche, Biogen and Calico under which we are working to identify and develop novel degraders across multiple therapeutic areas. We are also exploring additional strategic partnerships around certain targets, product candidates, and disease areas, which could advance and accelerate our research, allowing us to access additional capabilities and expand the utility of our TORPEDO platform.

### **Overview of Protein Degradation**

#### ***Protein Degradation***

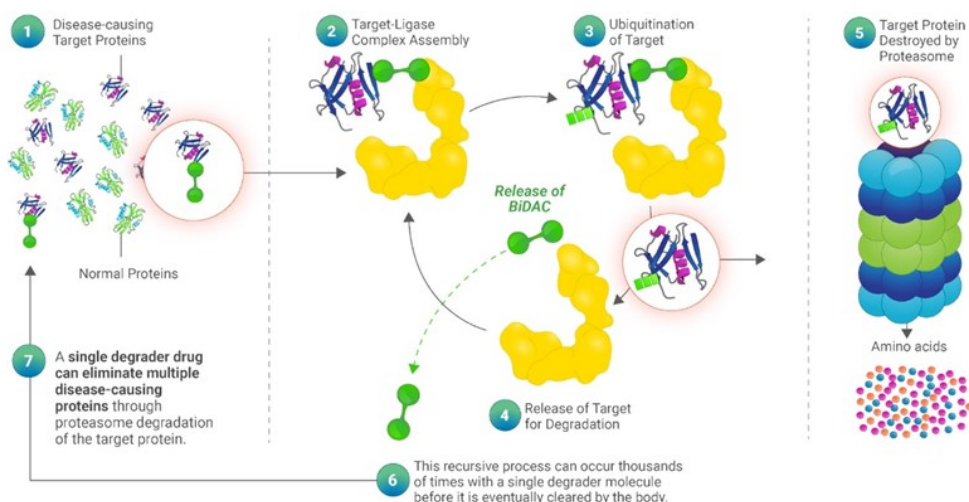
Proteins are large, complex molecules that play many critical roles in the human body. Due to their central role in biological function, protein interactions control the mechanisms leading to healthy and diseased states. Diseases are often caused by mutations that alter the normal function of proteins and in turn lead to protein dysfunction and then disease. Recent scientific advances continue to implicate the role of specific proteins in multiple disease states.

Protein levels within cells are controlled by a balance between their synthesis rate and their rate of degradation. Protein degradation provides a natural mechanism to maintain protein levels at a stable equilibrium, to remove aged or faulty proteins, or to rapidly eliminate the activity of certain regulatory proteins in response to specific signals. The human body has a highly conserved degradation machinery known as the ubiquitin proteasome system, or UPS, that can identify and break down proteins into their component amino acids. This process is mediated in part by a family of proteins called E3 ligases. The primary role of E3 ligases is to act as a quality control inspector by identifying proteins that are old, damaged, misfolded or otherwise deemed ready for degradation. When an E3 ligase identifies a target protein for degradation, it attaches a molecular tag called ubiquitin in a process called ubiquitination. This ubiquitination process typically continues until the target protein is tagged with multiple ubiquitins, known as poly-ubiquitination. Once the target protein is poly-ubiquitinated, it is released by the E3 ligase and is then quickly recognized by a proteasome, which is the cell's recycling plant. The proteasome degrades poly-ubiquitinated proteins into their component amino acids, and these amino acids can then be recycled to form new proteins or can be excreted by the cell. This process is illustrated in the following graphic.



Approximately five percent of all human genes are dedicated to encoding components of the ubiquitin-proteasome system. In addition, many proteins of therapeutic interest are often regulated by E3 ligases. Collectively, these factors underscore the essential role E3 ligases play in normal cellular function and how they can be leveraged against therapeutic protein targets.

Targeted protein degraders represent a novel modality that seeks to harness this natural degradation machinery to destroy disease-causing target proteins that E3 ligases would not otherwise target for destruction. The process of targeted protein degradation mediated by our degraders is illustrated in the graphic below.



Both our MonoDAC degraders and BiDAC degraders follow the same catalytic process, with the first step being the formation of a complex between the native E3 ligase, degrader and target protein, which we refer to as the ternary complex. This is shown in Step 2 in the above graphic for a BiDAC degrader. Formation of an appropriate ternary complex that can undergo ubiquitination results in poly-ubiquitination of the target in Step 3. Once the poly-ubiquitination process is complete for one molecule of a target protein, the degrader is released, as shown in Step 4, and then degradation of the target protein by the proteasome occurs in Step 5. Because the degrader is released unchanged, this recursive process—binding the target protein, ternary complex formation with the E3 ligase, poly-ubiquitination and release for degradation—can occur thousands of times with a single degrader molecule before it is eventually cleared by the body. Importantly, both the natural protein degradation process and the targeted protein degradation mediated by our degraders occur rapidly, on the order of milliseconds from initial target-ligase encounter to poly-ubiquitination and release for degradation by the proteasome. In this way, protein degraders act as a catalyst for a natural process and we refer to this process as the catalytic cycle, which is a crucial differentiator between degraders and traditional protein inhibitors, which must remain bound to the target protein to remain effective.

### ***Advantages of Targeted Protein Degradation Over Traditional Protein Inhibitors***

Many current targeted therapies are based on small molecules that inhibit the biological function of a protein of interest. One of the main limitations of inhibitor-based treatments is that sustained target occupancy levels are required for the inhibition of the biological function of protein, and thus efficacy. Since the pharmacological effect is driven by the drug exposure profile, the overall timing and duration of drug action is dependent on drug absorption, distribution, and elimination. These exposures can be challenging to achieve and may increase the likelihood of significant off-target side effects. A further limitation of this approach is the requirement to find compounds that bind to specific active sites on the protein that result in functional inhibition, as there are many sites on a target protein where small molecules can bind but have no effect on the overall function.

We believe targeted protein degradation is a novel modality that could offer significant potential benefits over traditional small molecule inhibitor approaches, including improved and sustained potency, fast and recursive catalytic effect, high selectivity, and an expansive target landscape.

#### ***Improved and Sustained Potency***

Degraders have the ability to offer a many-fold amplification of effect because a single degrader molecule can exert its effect recursively on a large number of target proteins. This ability of a degrader molecule to repeat its catalytic cycle multiple times is known as catalytic amplification. In contrast, traditional protein inhibitors rely on one-to-one binding of an inhibitor molecule with a target protein, with the protein only deactivated while the inhibitor is bound. This means that much higher concentrations of a protein inhibitor drug are needed to achieve the same level of therapeutic effect as a protein degrader.

In addition to requiring significantly less drug than a protein inhibitor, a degrader's impact on target protein function is more durable than that of a traditional inhibitor. This is because the activity of a target protein resumes as soon as an inhibitor is no longer bound to it, whereas a degrader completely eliminates its target protein and disease-causing activity is prevented until the cell is able to synthesize replacement proteins – a process that can take hours or even days. Therefore, in contrast to a typical reversible inhibitor, the effect of a degrader can persist well after it has been cleared from the body. The ability of a degrader to eliminate its target completely is another mechanism for improved potency relative to a traditional inhibitor. This is because a single protein can often have multiple functions, each mediated by a different domain. An inhibitor can only interfere with protein functions directly impacted by the region to which it binds. In the case of a disease-causing protein where more than one function contributes to pathogenic activity (for example, aberrant enzyme activity as well as ability to form multi-protein complexes), a degrader will eliminate all functions and therefore have a more profound effect versus an inhibitor that only blocks one. All these factors mean that degraders may help to achieve a more durable biological effect and better clinical outcomes.

#### ***High Selectivity***

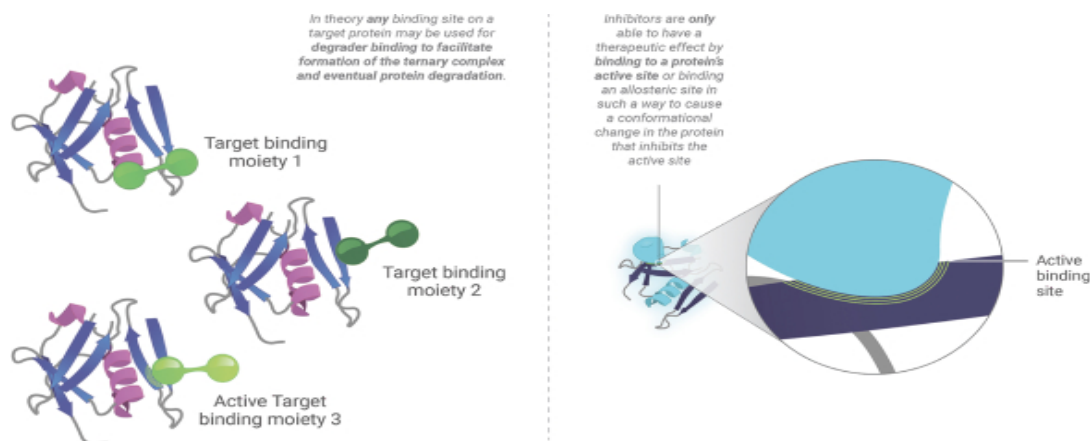
One of the primary challenges of protein inhibition is attempting to identify and develop molecules that only target cancerous cells or mutant proteins without having deleterious effects on normal cells or proteins, commonly referred to as off-target effects.

Each step in the protein degradation catalytic cycle requires specific positioning of the target protein and E3 ligase to progress through the cycle, and these positioning requirements can serve as filters to increase selectivity of a degrader molecule so that only the target protein is ultimately degraded, even if the degrader binds to multiple proteins. For example, degraders are created with the shape, or conformation, of the target protein in mind because a degrader and its target protein must assume a conformation amenable to forming a ternary complex with an E3 ligase. As a result, even if a degrader were to bind to a non-target protein, the resulting ternary complex may not have a conformation that is appropriate to facilitate ubiquitination and subsequent degradation. We are able to leverage these intrinsic properties of the ubiquitin-proteasome protein degradation pathway to design degraders to be highly selective for disease-causing target proteins.

#### ***Expansive Target Landscape***

Traditional inhibitors can only have a therapeutic effect if they are able to bind tightly to a site on a disease-causing protein that interferes with its function. This requires that the inhibitor binds directly to a protein's active site, or to an allosteric site in a way that leads to a conformational change that impairs protein activity. This inherently limits the number of druggable targets addressable with traditional inhibitors, as many potential binding sites are not in regions of a protein that interfere with function. In contrast, degraders can use any binding site on a protein to facilitate formation of a ternary complex with an E3 ligase that leads to its destruction. Additionally, whereas an inhibitor requires high affinity to its binding site to maintain occupancy and block function, degraders can interact with relatively weaker affinity in a transient fashion and still enable ubiquitination and destruction of the protein. Specifically, less than 15% of proteins are considered

druggable with traditional small molecule inhibitors because of limitations, including lack of accessible active binding sites. Targeted protein degradation greatly expands the potential target pool to include a significant proportion of those currently considered undruggable.



## Our Approach

We employ a comprehensive approach to product candidate discovery, selection, and development to maximize the potential therapeutic benefit of our protein degraders. We seek out indications with high value protein targets that may benefit the most from degraders, with catalytic degradation turnover as the key metric by which to assess protein degradation. To that end, we have invested heavily in experimental tools, computational and predictive models, and team expertise to analyze and optimize the catalytic ability of our degraders through our TORPEDO platform. Additionally, we leverage our platform to optimize the ability of our degraders to initiate the ubiquitin-proteasome protein degradation cycle and predict their function *in vivo*. Due to the rapid optimization allowed by our TORPEDO platform and the ability of our platform to predict degrader effects *in vivo*, we are able to quickly and efficiently advance programs from target identification to the candidate development stage.

## Our TORPEDO Platform

Our proprietary platform, TORPEDO, allows for informed and efficient drug design and discovery through a robust chemistry engine and proprietary assays, culminating in predictive models that enable us to maximize catalytic turnover and predict *in vivo* performance. Key elements of the platform include:

- **Focus on Catalytic Efficiency:** We seek to optimize catalytic degradation turnover by focusing our analytical techniques and predictive models on the relationship between degrader properties and ultimate protein degradation. Our degraders are designed to activate the E3 ligase and facilitate target protein binding and ubiquitination, resulting in rapid overall target degradation. The ability of our degraders to repeat this process recursively, with the same single degrader molecule interacting with many copies of the target protein, allows us to optimize our product candidates for catalytic degradation turnover and, as a result, create candidates that have the potential to provide a greater therapeutic effect. Our MonoDAC degraders and BiDAC degraders need to achieve sufficient binding affinity to initiate brief ternary complex formation, but, unlike traditional inhibitors, they do not need to achieve prolonged stable binding to achieve desired physiological effects. In a number of our preclinical research activities, we have observed that even weaker binders can still result in very efficient degraders since they may allow for higher rates of catalytic degradation turnover, which is something we prioritize to achieve potentially greater activity.
- **Ability to design, analyze and predict degrader performance:** We have made a significant investment in computational methods and tools to enhance our ability to rationally design degraders. *In silico* models allow us to design degraders with enhanced potency and selectivity across our pipeline. Additionally, our cellular degradation assays provide high-quality data that we analyze using a proprietary and unique framework based on fundamental enzymology principles, which allow us to predict both the depth and duration of target degradation at any dose *in vivo*.
  - We have developed high-throughput cellular degradation assays that are designed to produce quantitative data showing the relationship between degrader concentration and This approach allows protein degradation quantitation with greater precision and higher throughput than traditional western-blot approaches. The application of our experimental data to our proprietary models then

allows us to predict protein degradation kinetics and allows us to rapidly iterate and improve on degrader candidates and design for properties that optimize catalytic degradation turnover.

- We have also established an enzymology framework that assesses and balances the relationship between degrader concentration, time, and target protein degradation to identify the key kinetic parameters of degrader induced protein degradation. We have extended this framework to proprietary PK/PD models, which integrate these kinetic parameters with metabolism and PK exposure profiles to predict *in vivo* degrader performance. Our predictions of degrader performance are routinely validated through *in vivo* PD experiments with measurements of target degradation from tumor samples using standard western blot assays. We have observed that these models linking cellular assays with predicted *in vivo* performance have significantly accelerated our discovery process, and we believe that this will increase the likelihood of successfully transitioning from preclinical models to the clinic.
- **Investment in Cereblon:** Our lead degraders exclusively utilize Cereblon as the E3 ligase. There are over 600 E3 ligases in the human proteome, of which the biology has been well characterized in no more than 50. A limited number of E3 ligases, including Cereblon, VHL, MDM2, IAPs and  $\beta$ -TRCP, have been reported to be suitable for targeted protein degradation. We have chosen to focus on Cereblon as the E3 ligase target of our protein degradation approach for several reasons:
  - Extensive clinical experience with the approved drugs thalidomide, lenalidomide and pomalidomide has shown that using Cereblon can effect target degradation. The mechanism of action of these molecules is to degrade disease targets, specifically IKZF1 and IKZF3, by bringing them into complex with Cereblon. Lenalidomide and pomalidomide are both approved drugs that have served as part of the standard of care for the treatment of MM for the last 17 and 10 years, respectively. Together, this experience clinically validates that Cereblon has been harnessed by other drugs.
  - Cereblon is widely expressed across tissues and is present in all cellular compartments, including the cytoplasm and nucleus, potentially allowing for Cereblon-mediated targeted protein degradation across a wide variety of clinical settings and potential targets.
  - We have developed multiple distinct, proprietary Cereblon binders that we have designed for improved drug-like properties, such as enhanced oral bioavailability, solubility, permeability, and stability, and all of our product candidates and programs benefit from these properties of our proprietary Cereblon binders. Our library of Cereblon binders offers a proprietary and powerful toolkit for degrader discovery. This Cereblon binder toolkit enables a more modular approach to identifying and optimizing degraders, as each of these binder classes encode distinct drug-like properties and, importantly, unique “exit trajectories” from the Cereblon surface following protein degradation, which can promote better target degradation turnover.
- **Ability to develop both MonoDAC and BiDAC degraders:** Our platform provides the flexibility to address different classes of disease-causing proteins with a tailored approach. For those target proteins where a binding site exists, we can develop BiDAC degraders leveraging our Cereblon toolkit. For target proteins where a binding site is not present or lacks sufficient specificity, such as transcription factors, we can leverage our proprietary MonoDAC library of over 7,000 compounds to screen for hits against the target. Once we have a confirmed hit on a target, we are able to leverage the other elements of our TORPEDO platform to optimize either a MonoDAC or a BiDAC degrader.

These features help focus our platform on the creation of product candidates that we believe will present minimized biology and toxicity risk, while also addressing unmet medical needs.

### **Our Product Candidates—Highly Potent and Selective Targeted Protein Degraders**

We currently have a number of product candidates in development. We are currently conducting first-in-human Phase 1/2 clinical trials of CFT7455, CFT8634 and CFT1946. These programs are directed towards targets that remain inadequately treated with available therapies or are undruggable.

#### ***CFT7455: A IKZF1/3 Degradar for Multiple Myeloma and non-Hodgkin's Lymphoma,***

We are developing CFT7455, an orally bioavailable degrader designed to target IKZF1/3, for the treatment of MM and NHLs. We have chosen IKZF1 and IKZF3 as our initial targets for degradation because of their strong mechanistic rationale and well-defined biology. In preclinical studies, CFT7455 has shown robust activity in MM, PTCL, and MCL subcutaneous xenograft mouse models, providing preclinical proof of concept. Specifically in MM, we have observed in preclinical studies that CFT7455 remains active in *in vivo* and *in vitro* models that are relatively insensitive to standard of care agents that have a similar mechanism of action, such as pomalidomide. We believe that the differentiated

pharmacology of CFT7455, including its high potency, may translate into significantly improved clinical outcomes in each of the indications in which we are pursuing its development.

In April 2022, we presented clinical data from Arm A of our ongoing CFT7455 Phase 1/2 clinical trial. These data showed that single agent CFT7455 resulted in deep and durable degradation of IKZF1/3, as quantified by mass spectrometry, and meaningful decreases in serum free light chain (dFLC); per criteria established by the International Myeloma Working Group, dFLC is a defining characteristic of responsiveness. Neutropenia, a known on-target toxicity associated with IKZF1/3 degraders, was dose-limiting at the 50 µg daily dose on a dosing schedule with a seven-day drug holiday over a 28-day cycle. As a result, we modified the dosing schedule to include a 14-day dose holiday over a 28-day cycle, and the dose was reduced to 25 µg to establish a safe dose at the new schedule from which to escalate.

We continue to enroll patients in the Phase 1 dose escalation portion of the ongoing Phase 1/2 clinical trial, which is designed to capitalize on potential opportunities for expedited product development and accelerated approval in MM and NHL.

#### *IKZF1 and IKZF3 Are Well Understood Biological Targets for Certain Blood Cancers*

IKZF1 and IKZF3 are transcription factors central to the differentiation of lympho-myeloid multipotent progenitor cells through mature immune cells, including T cells and plasma cells, such as B cells. In particular, by preventing the maturation of B cells there is an antiproliferative effect in B-cell driven blood cancers, such as MM, B-cell lymphomas, and myelodysplastic syndrome. In addition to these cell-intrinsic dependencies on IKZF1/3 for B cell maturation, degradation of IKZF1 and IKZF3 has been shown in third-party research to lead to enhanced IL-2 expression in T cells, meaning IKZF1/3 degradation also induces T cell activity and may exert anti-cancer effects. Further, IKZF1/3 has been previously validated as a target in clinical practice as lenalidomide and pomalidomide primarily target IKZF1/3 as their mechanism of action.

#### *Multiple Myeloma*

In the United States, MM represents nearly 1.8% of all new cancer cases. The National Cancer Institute estimated that there were 34,470 new cases of MM in the United States and 12,640 deaths from the disease in 2022. Although overall outcomes for patients with MM have improved substantially over the past several decades, patients with MM have a poor prognosis and the predicted median five-year relative survival rate is only 57.9%. As such, there remains a significant unmet need.

Most patients with MM will have an initial response to treatment. Based on fluorescence in situ hybridization, or FISH, studies on bone marrow, patients are stratified into high-risk or standard-risk categories. High-risk patients eligible for hematopoietic cell transplantation receive induction therapy with a combination regimen, often including an IKZF1/3 targeting drug like lenalidomide, to reduce the number of tumor cells prior to stem cell collection. Alternatively, patients who are ineligible for hematopoietic cell transplantation immediately receive a combination regimen, often with three to four classes of drugs, including an IKZF1/3 targeting drug and a steroid, typically dexamethasone, until progression or unacceptable toxicity.

However, current therapies are not curative, and most patients will ultimately progress. Despite the likelihood of an initial remission, there is a significant unmet need because most patients experience serial relapse and will be treated with most available agents at some point during their disease course. In our clinical program, we will initially focus on treating patients with relapsed or refractory MM who have received at least three lines of specified prior therapy, including lenalidomide, pomalidomide, proteasome inhibitors and an anti-CD38 monoclonal antibody, or mAb. Ultimately, our intention is to seek approval in earlier lines of therapy, replacing or complementing current IKZF1/3 targeting drugs. We believe that the high potency and activity we have seen *in vivo* has the potential to translate into a meaningful benefit for patients.

#### *Peripheral T-cell Lymphomas*

PTCLs are a heterogeneous and typically aggressive group of NHLs. The Surveillance, Epidemiology and End Results Program or SEER Program, of the National Institutes of Health, or NIH, estimated that there were 80,470 new cases of NHL in the United States and 20,250 deaths from the disease in 2022. PTCLs comprise approximately 4% of all NHLs in the United States and Europe, with an incidence that increased from 0.1 cases per 100,000 in 1992 to 0.4 cases per 100,000 in 2006, potentially reflecting improved diagnostic methods. The five-year overall survival of patients with PTCL is 30-50%.

PTCL is a heterogeneous malignancy with many subtypes and while the outcomes in these subtypes vary, many patients with PTCL do poorly. For example, in patients with PTCL in whom no subtype is defined, which is often referred to as PTCL not otherwise specified or PTCL-NOS, the five-year overall survival is approximately 20% to 32%. Further, patients with angioimmunoblastic, natural killer/T-cell lymphoma, adult T-cell leukemia/lymphoma, hepatosplenic, enteropathy type or ALK-peripheral T-cell lymphoma all have a median five-year overall survival of less than 50%. Although initial

overall response rates for chemotherapy are approximately 40% to 75%, most patients ultimately relapse. Median progression free survival, or PFS, following chemotherapy is 12 to 14 months, with a median five-year survival rate of approximately 20% to 30%. Lenalidomide has been tested clinically in PTCL in a Phase 2 clinical trial and shown to have an overall response rate of 22% to 26%. However, Cereblon modulators such as lenalidomide are not widely used nor approved for treating PTCL. Based on our preclinical data, we believe CFT7455 has the potential to create a meaningful benefit for these patients and become an established standard of care for these patients, if approved.

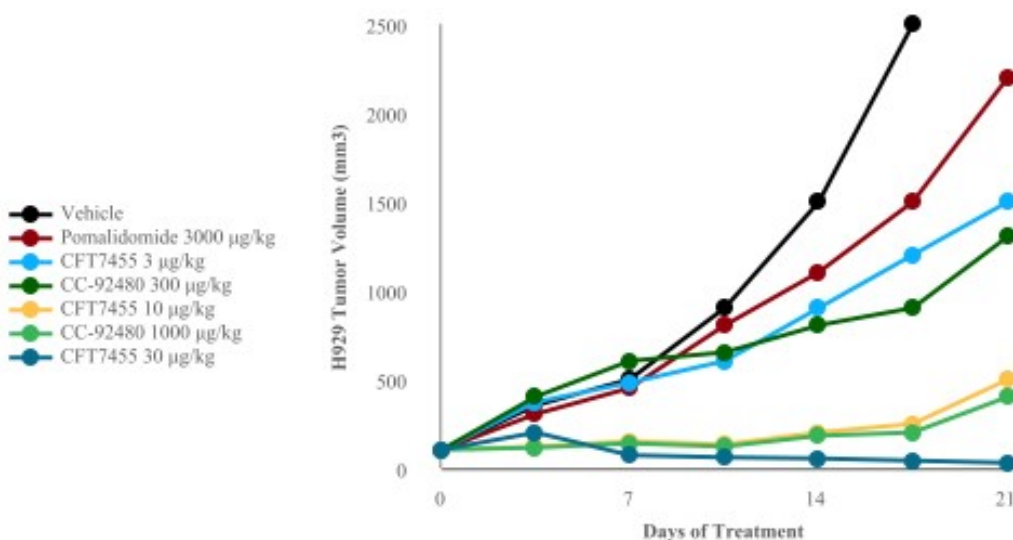
#### Mantle Cell Lymphoma

MCL is one of the mature B-cell NHLs and comprises approximately seven percent of adult NHLs in the United States and Europe, with an incidence of approximately 0.8 cases per 100,000 persons per year according to 2021 SEER Program estimates. Median overall survival for patients receiving intensive therapy is four to five years. Outside of agents being tested in clinical trials, front-line treatment options typically include some combination of conventional chemoimmunotherapy, rituximab, and radiation therapy. Most patients with MCL experience serial relapse and are treated with various agents, including IKFZ1/3-targeting drugs, BTK inhibitors, or the BCL-2 inhibitor venetoclax. Lenalidomide is approved for use in patients with MCL whose disease has relapsed or progressed after two prior therapies, one of which included bortezomib, based in part on an observed overall response rate of approximately 26%. However, lenalidomide is not widely used to treat MCL. Accordingly, we believe that CFT7455 has the potential to meaningfully improve outcomes and become an established standard of care for these patients, if approved.

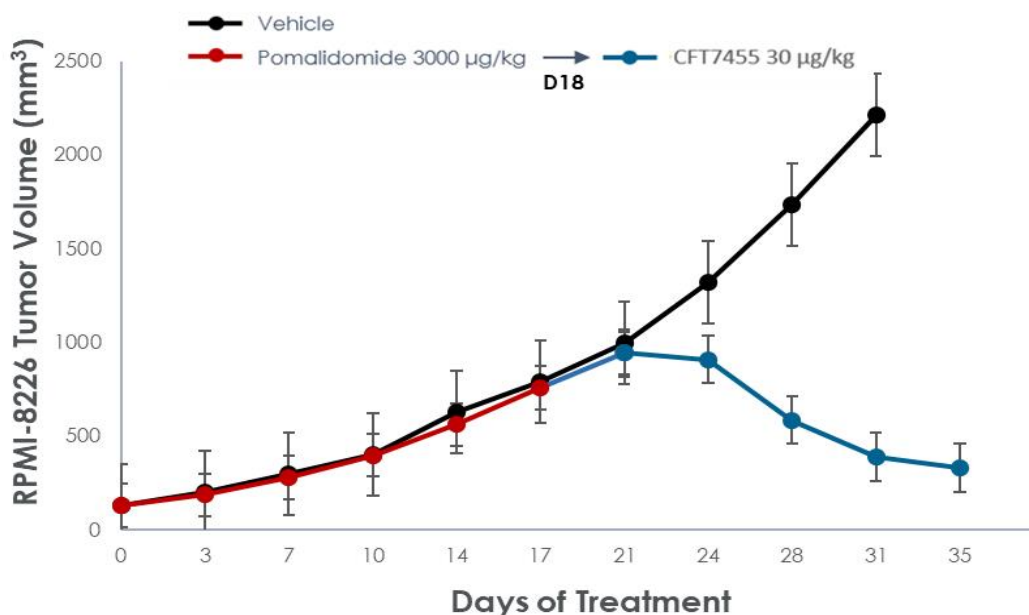
#### Preclinical Development

We have conducted comprehensive preclinical analysis across multiple mouse models to study CFT7455 as a potential treatment for MM, PTCL and MCL.

We have observed potent activity for CFT7455 *in vitro* across a panel of relevant cell lines. In multiple subcutaneous xenograft mouse models of MM, PTCL and other NHLs, CFT7455 treatment resulted in complete regression, as shown in the graphs below. Significantly, 30  $\mu\text{g}/\text{kg}$  of CFT7455 administered once daily, or QD, demonstrated complete regression and clear dose responsiveness in a widely used MM xenograft model, H929, as shown in the graph below.



In the RPMI-8226 MM xenograft, we observed that pomalidomide at the clinically relevant dose of 3,000 µg/kg was indistinguishable from treatment with the vehicle as shown in the graphic below. A low dose of CFT7455, 30 µg/kg, was active in the model, even when administered to large tumors that had grown despite treatment with 3,000 µg/kg of pomalidomide for 21 days and were insensitive to pomalidomide and then were switched to treatment with CFT7455.



#### *Our First-in-Human Phase 1/2 Trial*

In June 2021, we initiated a first-in-human Phase 1/2 clinical trial for CFT7455, and continue to enroll patients. This trial is designed to primarily investigate safety, tolerability, and anti-tumor activity. Secondary and exploratory objectives are to characterize the PK and PD profile of CFT7455. The Phase 1 portion of the study explores CFT7455 as a single agent in patients with relapsed or refractory MM and NHL, as well as in combination with dexamethasone in patients with relapsed or refractory MM. We continue to enroll patients in the Phase 1 dose escalation portion of this ongoing Phase 1/2 clinical trial.

Following identification of a recommended dose(s) and schedule(s), the Phase 2 portion of the trial is expected to expand to the following four investigational arms: (1) in relapsed or refractory MM, single agent CFT7455; (2) in relapsed or refractory MM, CFT7455 combined with dexamethasone; (3) in peripheral T-cell lymphoma, single agent CFT7455; and (4) in mantle cell lymphoma, single agent CFT7455.

#### ***CFT8634: A Novel BRD9 Degradator for Synovial Sarcoma***

We are developing CFT8634, an orally bioavailable protein degrader targeting BRD9 for the treatment of synovial sarcoma and SMARCB1-null solid tumors. We have chosen BRD9 as a target for our approach because of the strong mechanistic rationale, well-defined biology, unique opportunity to target BRD9 with a degrader (as compared to traditional protein inhibitors, which are ineffective in this setting), and significant unmet need in these patient populations. Specifically, there is limited benefit of existing treatments for metastatic or locally advanced synovial sarcoma, with patients experiencing progression-free survival of approximately seven months in the front-line setting and approximately five months in the relapsed or refractory setting. We are pursuing clinical development to treat patients with SMARCB1-null solid tumors and synovial sarcoma, which is defined by a gene translocation SS18-SSX that results in dependency on BRD9 and is therefore potentially addressable by a BRD9 degrader. We believe that the ability of our degrader CFT8634 to drug BRD9 has the potential to offer a benefit over currently available therapies for patients with synovial sarcoma.

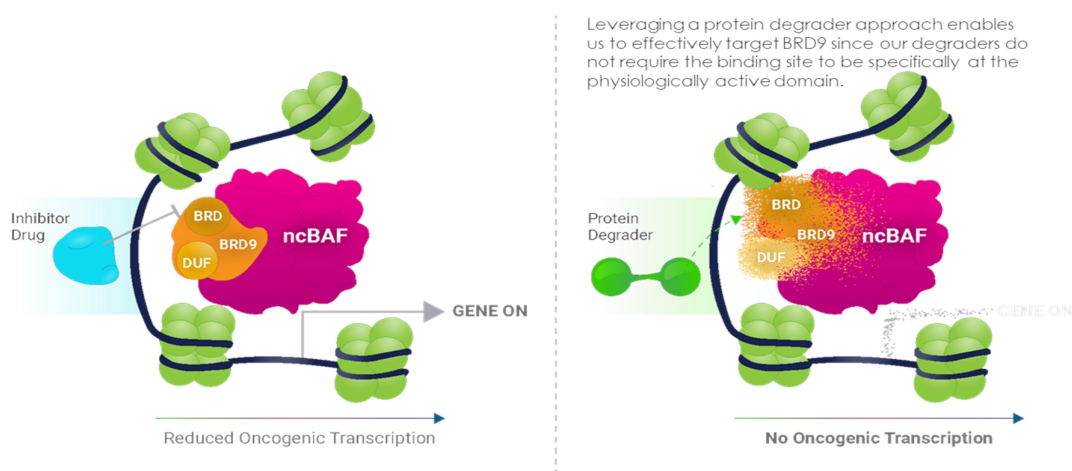
Assuming CFT8634 has a favorable profile in these early clinical trials, we intend to discuss with the FDA the potential registration pathway in patients with synovial sarcoma and SMARCB-1 null solid tumors, including the possibility of accelerated approval.



### ***BRD9 Is a Well Characterized Driver of Cancer with No Currently Available Targeted Therapies***

BRD9 is a component of the ncBAF complex, which is one of three types of BAF complexes in human cells. The BAF complexes, also known as SWI/SNF complexes, are responsible for regulating gene transcription. Critically, BRD9 and the ncBAF complex of which it is a component, is not normally required for cell survival. Instead, normal cells rely on another complex, cBAF, for cellular growth, and BRD9 is not a member of this complex. However, in certain genetic settings, ncBAF drives malignancy and the resulting tumors are dependent on BRD9. Genetic settings in which BRD9 is critical share the same feature: the function of the cBAF complex is compromised because SMARCB1, a critical component for normal function of the cBAF complex, is removed from the complex. This situation, referred to as BAF perturbation, is seen in both cancers in which SMARCB1 is deleted, such as malignant rhabdoid tumors, or MRTs, and epithelioid sarcoma, as well as when a pathogenic fusion protein referred to as SS18-SSX results in the ejection of SMARCB1 from the BAF complex. This SS18-SSX fusion protein is the defining genetic lesion that drives synovial sarcoma. In each of these settings, BAF perturbation results in a central dependency on the ncBAF complex, and as a result BRD9, for tumor growth. This is an example of synthetic lethality, in which the cancer cell has a specific vulnerability to BRD9 degradation in the setting of the underlying genetic lesion. In contrast, normal cells, which do not harbor this genetic lesion, are relatively unaffected by the degradation of BRD9. As a result, BRD9 is a critical dependency of the cancer in these genetic settings and depriving the cancer cell of BRD9 effectively stops tumor growth.

BRD9 has previously been considered undruggable because existing small molecule inhibitors of the bromodomain are inactive against synovial sarcoma because, preclinically, inhibition of this domain is not sufficient to block BRD9 from driving cancer cell growth. Inhibitors of other protein functions, such as that of the critical domain of unknown function, or DUF, have not been described. We therefore believe that our approach to targeted protein degradation of BRD9 has the potential to offer a major benefit over currently available therapies for synovial sarcoma and SMARCB1-null solid tumors.



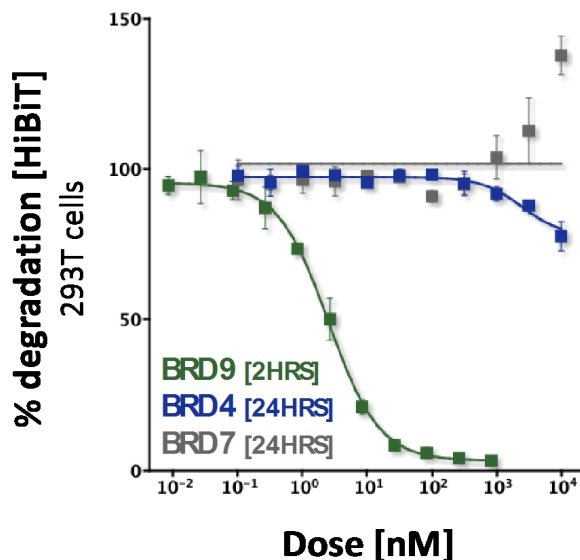
Synovial sarcoma is an aggressive tumor that accounts for approximately 900 cases in the United States each year, or approximately 10% of all soft tissue sarcomas. Like many sarcomas, synovial sarcoma is characterized by recurrent chromosomal arrangements and is referred to as a fusion gene driven malignancy. Specifically, nearly all synovial sarcomas contain a fusion of the SS18 gene on chromosome 18 to the SSX1, SSX2 or SSX4 gene on the X chromosome. This type of mutation is referred to as a t(X;18) chromosomal rearrangement, or an SS18-SSX fusion.

#### ***SMARCB1-null Solid Tumors***

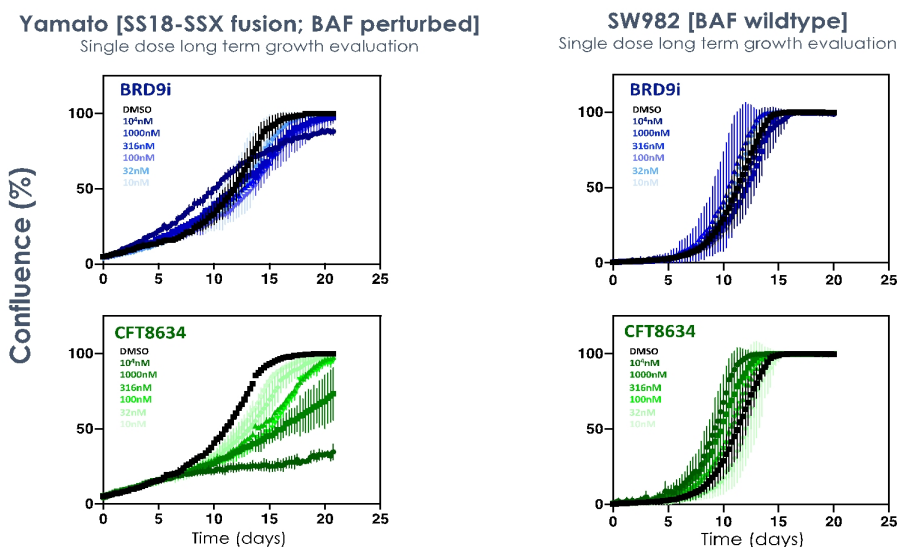
SMARCB1 is a key member of the BAF chromatin-remodeling complex and assists in the control of gene transcription. The function of SMARCB1 and the BAF complex in cancer has only recently been established. SMARCB1 is a tumor suppressor gene, meaning any decrease in function could potentially result in tumor proliferation. The inactivation of both alleles of SMARCB1 has been shown to result in several types of tumors, including MRTs, as well as epithelioid sarcoma, renal medullary carcinoma, undifferentiated pediatric sarcomas, a subset of hepatoblastomas, and others.

#### ***Preclinical Development***

We have conducted preclinical studies of CFT8634 in two mouse models. CFT8634 was highly selective for BRD9 relative to other bromodomain containing proteins, including BRD7 and BRD4, as shown in the dose dependency of target degradation in H293T cell lines expressing the individual proteins, as reflected in the graphic below.

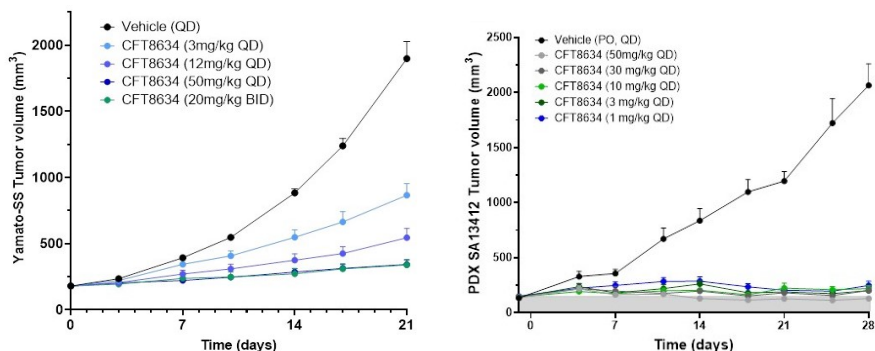


We have also observed meaningful *in vitro* dose-dependent inhibition of cell proliferation of synovial sarcoma cell lines over time. Here, cell proliferation is measured by analyzing the occupied area of cells in a sample over time where densely packed cells are considered confluent. Cell growth inhibition was evidenced in cultures that show a growth plateau below 100%. The figure below on the left shows the effect of CFT8634 on BAF perturbed Yamato cell lines, which is a mouse xenograft model of synovial sarcoma, compared to the effect of a BRD9 inhibitor, shown as BRD9i or the vehicle, dimethylsulfoxide, or DMSO, which were ineffective. As demonstrated in the figure on the right below, CFT8634 had little impact on the growth of a BAF wildtype SW982 cell line, demonstrating that its effect was limited to cells with BAF perturbation.



The below graphic shows CFT8634 was active when dosed orally in a mouse xenograft model of synovial sarcoma (Yamato) and a PDX model (SA13412), with dose dependency observed between 3 mg/kg and 50 mg/kg QD, as well as

20mg/kg twice daily dose, or BID, for Yamato, and 50 mg/kg QD, 25mg/kg BID, and 16.6 mg/kg three times daily for PDX.



### *Our First-in-Human Phase 1/2 Clinical Trial*

In May 2022, we initiated a first-in-human Phase 1/2 clinical trial for CFT8634 and continue to enroll patients in this ongoing clinical trial. The Phase 1 portion of the trial will primarily investigate the safety and tolerability of CFT8634 as a monotherapy in patients with synovial sarcoma or SMARCB1-null solid tumors. Following identification of a recommended dose(s) and schedule(s), we expect to enroll two expansion cohorts, both to explore CFT8634 as a monotherapy, with one cohort to enroll patients who are known to have synovial sarcoma, and a second that will be comprised of patients with SMARCB1-null solid tumors.

In May of 2022, we initiated a Phase 1/2 clinical trial of CFT8634 in synovial sarcoma and SMARCB1-null solid tumors. In January 2023, we shared initial PK and PD data from the first three dose escalation cohorts (2 mg, 4 mg, and 8 mg once daily) of the Phase 1/2 clinical trial. These data showed dose proportional exposure, strong oral bioavailability, and deep BRD9 degradation. We continue to enroll patients in the Phase 1 dose escalation portion of the ongoing Phase 1/2 clinical trial.

### ***CFT1946: Degrading BRAF V600 to Treat Melanoma, Colorectal, and Non-small Cell Lung Cancers***

We are developing CFT1946, an orally bioavailable degrader of BRAF V600. We selected BRAF V600 as a target due to its strong mechanistic rationale, well-defined biology, and unmet need. In the United States, BRAF mutations occur in approximately 5% of all cancers, which translates to approximately 100,000 patients diagnosed with BRAF mutated cancers annually. Approximately 70 to 90% of all BRAF mutations are V600. We plan to initially pursue development of CFT1946 in three types of cancers: melanoma, in which BRAF V600 mutations occur in approximately 35% of late-stage patients; colorectal, in which BRAF V600 mutations occur in approximately 5 to 10% of patients; and NSCLC, in which BRAF V600 mutations occur in approximately 1-2% of patients. In patients, there remains a high unmet need for those who relapse after, or do not respond to, approved BRAF inhibitors. We believe that a mutant-specific BRAF V600 degrader could offer a significant mechanistic benefit over currently available BRAF inhibitors and could have the potential to confer significant improvements in clinical outcomes.

### ***BRAF V600 is a Common and Well Understood Oncogenic Mutation***

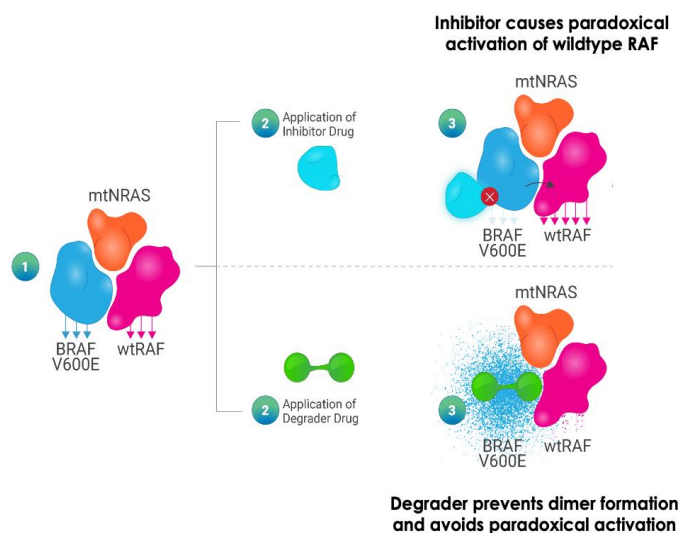
BRAF is one of several protein kinases involved in a signaling cascade to initiate cell proliferation, known as the mitogen-activated protein kinase, or MAPK, pathway. The MAPK pathway conducts extracellular proliferative signals to the nucleus of cells, signaling them to proliferate. Many cancers are characterized by activating mutations in components of this MAPK pathway, including BRAF V600 mutations, which confer constitutive activation of the MAPK pathway and promote oncogenic transformation and can cause tumor growth.

Single base substitutions for the amino acid valine at codon 600 in the BRAF gene, referred to as V600, are known as Class I mutations and when those V600 mutations result in substitution of glutamic acid for valine (the most common such mutation), they are referred to as V600E mutations.

BRAF V600 mutants activate the MAPK pathway constitutively, meaning that cell proliferation is activated without receiving the extracellular proliferative signals necessary to activate the pathway normally. Constitutive activation occurs because BRAF V600 mutants are able to signal as a single protein, or a monomer, while wild type BRAF proteins must form a complex of two proteins, or a dimer, before downstream signaling can occur. This constitutive activation leads to overactivation of the MAPK cell proliferation pathway, causing oncogenic cell proliferation and tumor growth. Approved small molecule inhibitors of BRAF V600—vemurafenib, dabrafenib, and encorafenib—block the constitutive activation of

the MAPK pathway by the mutant BRAF monomer. However, BRAF inhibition with these molecules can lead to an alternative activation of the MAPK pathway, known as paradoxical activation. Under these conditions, BRAF inhibitors bind and inhibit BRAF V600, but this inhibited form can form a protein dimer with other RAF proteins, including both wild type BRAF and BRAF mutants, activating the second molecule for signaling. This BRAF driven paradoxical activation activates, rather than inhibits, the MAPK pathway. For this reason, BRAF inhibitors are frequently used in combination with inhibitors of MEK, a protein downstream of BRAF in the MAPK pathway, which improves response rates and clinical outcomes. However, patients frequently do not respond sufficiently, or they develop resistance to this approach. Many known mechanisms of resistance to approved BRAF inhibitors result in the promotion of BRAF dimerization and, in these settings, the current BRAF inhibitors are ineffective.

We believe that targeted protein degradation of BRAF V600 mutations offers the potential for a fundamental improvement over current BRAF inhibitors due to the advantages of degraders over inhibitors in general and because degrading mutant BRAF removes the possibility of incorporation into a BRAF dimer and subsequent paradoxical activation.



### Melanoma

According to the National Cancer Institute, approximately 100,000 patients were diagnosed with melanoma in 2022 in the United States, and approximately 4% of those cases, or about 4,000 patients per year, will have locally advanced or metastatic disease at diagnosis. Moreover, approximately 35% of late-stage melanoma patients carry BRAF mutations, approximately 90% of which are BRAF V600E mutations. Taken together, we estimate that there are over 5,000 newly diagnosed melanoma patients in the United States per year with BRAF V600E-mutated locally advanced or metastatic disease.

The recommended first-line treatment for patients with BRAF V600E-mutated unresectable or metastatic melanoma is anti-PD-1 monotherapy, such as pembrolizumab or nivolumab, or combination therapy with a BRAF inhibitor, such as dabrafenib, vemurafenib or encorafenib, and a MEK inhibitor, such as astrametinib, cobimetinib or binimetinib. However, a significant number of patients undergoing this combination therapy do not sufficiently respond or do not have a durable response as resistance to the therapy occurs. Specifically, across several double-blind randomized controlled trials conducted by others evaluating BRAF and MEK inhibitor combination therapy in patients with previously untreated locally advanced or metastatic melanoma, the median PFS has ranged from 9.9 to 14.9 months. After each of these lines of therapy is used, there are no approved single-agent therapies that effectively target BRAF. In preclinical models of resistance to BRAF inhibition, our degraders remained active when dosed in combination with a MEK inhibitor, in contrast to the approved BRAF inhibitor, encorafenib, which is inactive in this setting. As a result, a BRAF V600 degrader may be active clinically in the setting of resistance to approved BRAF inhibitors.

### Colorectal Cancer

According to the National Cancer Institute, approximately 150,000 patients in the United States were diagnosed with colorectal cancer in 2022. Of these patients, approximately 20%, or about 30,000 patients, were diagnosed with metastatic disease and approximately 25%, or about 37,000 patients, were diagnosed with local disease that will recur with metastases. Between 5 and 10% of colorectal cancers, or about 7,500 to 15,000 cancers annually, harbor a BRAF V600 mutation.

Patients with BRAF V600 mutations who have progressed on prior therapy may receive a combination therapy of encorafenib and cetuximab, both inhibitor therapies. However, this therapy regimen has limited efficacy; the median PFS is approximately 4.2 months.

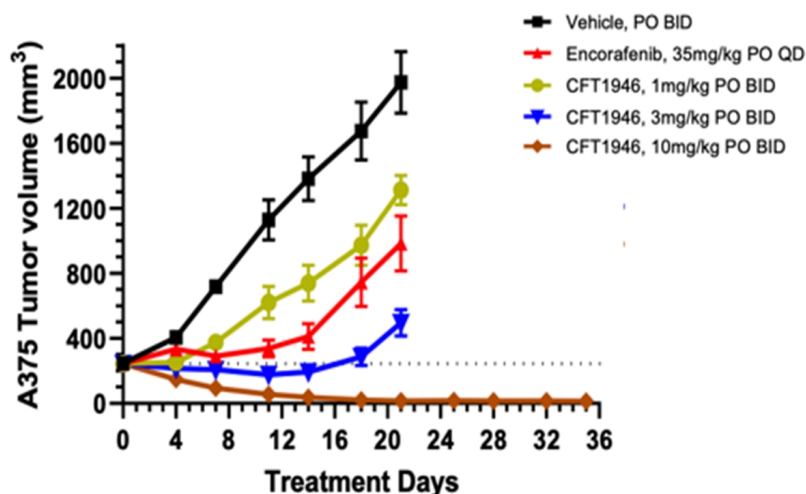
#### *Non-Small Cell Lung Cancer*

According to the National Cancer Institute, approximately 195,000 patients in the United States were diagnosed with NSCLC in 2022. Of these patients, approximately 40%, or 78,000 patients, were diagnosed with metastatic disease with high recurrence rates of locally diagnosed tumors. Approximately 1-2% of NSCLC patients, or 1,950 to 3,900 patients, have a BRAF V600 mutation.

NSCLC patients who are newly diagnosed with a BRAF V600 mutation are typically treated with the combination therapy dabrafenib plus trametinib, both inhibitor therapies, typically have a median PFS of 15.2 months. Patients who have received prior therapies to treat a BRAF V600 mutation and then receive the dabrafenib and trametinib combination typically have a median PFS of 9 months.

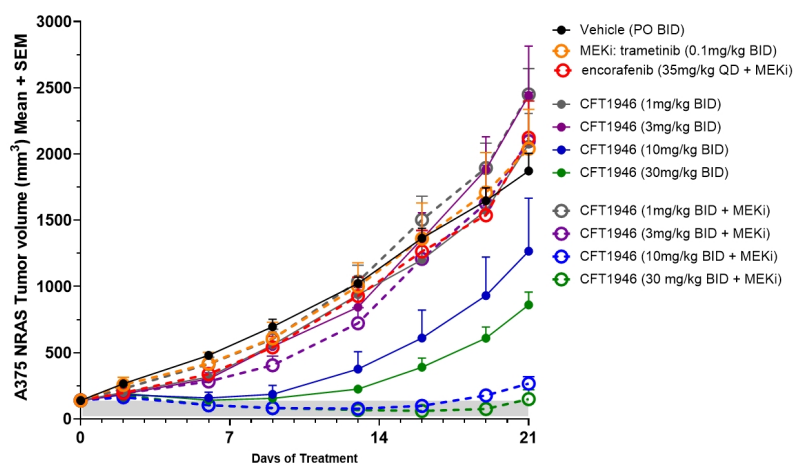
#### **Preclinical Development**

In preclinical studies, in the A375 BRAF V600E melanoma model, we have observed that our development candidate CFT1946 showed a dose-dependent reduction in tumor growth and demonstrated tumor regression at the minimum efficacious dose of 10 mg/kg administered orally twice daily. Further, CFT1946 at doses starting at 2mg/kg (PO, BID) all demonstrated superior activity to encorafenib, an FDA approved BRAFV600 inhibitor. Additionally, there were no adverse effects (assessed by significant loss of body weight) observed in the xenograft study shown below.



We have further demonstrated superior efficacy of CFT1946 in the BRAF<sup>i</sup> resistant A375 model (BRAF V600E + NRAS-Q61K) compared to the MEK inhibitor trametinib alone or in combination with encorafenib. The NRAS Q61K activating mutation is a clinically observed mechanism of resistance to BRAF inhibitors. Treatment of xenograft tumors with 10 mg/kg (PO, BID) in combination with 0.1 mg/kg trametinib displayed complete tumor growth inhibition while treatment with encorafenib and trametinib did not provide any significant tumor growth inhibition. We did not observe any adverse effects

of treatment with CFT1946 in combination with trametinib (as assessed by no significant changes to mouse body weight) in our xenograft study.



### *Our First-in-Human Phase 1/2 Clinical Trial*

In January 2023, we initiated a first-in-human Phase 1/2 clinical trial for CFT1946 and continue to enroll patients in this ongoing clinical trial. The Phase 1/2 clinical trial will primarily investigate safety, tolerability, and anti-tumor activity, with secondary and exploratory objectives to characterize the PK and PD profile of CFT1946. The initial arm of the Phase 1 portion of the study will evaluate CFT1946 as a single agent in patients with BRAF V600 solid tumors including colorectal cancer, melanoma, and NSCLC after prior BRAF inhibitor treatment. As the Phase 1 trial progresses, an additional arm of the trial will evaluate CFT1946 in combination with trametinib in patients with BRAF V600 solid tumors including colorectal cancer, melanoma, and NSCLC after prior BRAF inhibitor treatment. Following the identification of the recommended dose, the Phase 2 portion of the trial is expected to expand to three investigational arms to evaluate: (1) CFT1946 monotherapy in patients with V600 mutant melanoma or NSCLC after prior BRAF inhibitor treatment; (2) CFT1946 in combination with trametinib in patients with V600 mutant melanoma or NSCLC after prior BRAF inhibitor treatment; and (3) CFT1946 in combination with trametinib in patients with V600 mutant NSCLC who have not previously been treated with a BRAF inhibitor.

### ***CFT8919: Potent, Oral, Allosteric, Mutant-selective Degradator of EGFR L858R***

We are developing CFT8919, an orally bioavailable allosteric degrader of EGFR L858R for the treatment of NSCLC. We have chosen EGFR because of its well-defined biology and the limitations that EGFR kinase inhibitors face that we believe our degrader approach may be able to overcome. Our initial target population is patients with EGFR L858R driven NSCLC who have progressed after treatment with approved EGFR inhibitors, including osimertinib. We believe CFT8919 has the potential to overcome resistance to standard of care EGFR inhibitors to effect deeper and more durable responses due to the unique advantages of protein degradation.

### ***EGFR is a Well-Characterized Protein Target for Oncology with Known Resistance Mechanisms***

EGFR is a receptor tyrosine kinase that is involved in cell signaling pathways that control cell division and survival. Mutations in the EGFR gene cause the EGFR protein to signal aberrantly in some types of cancer cells, including a subset of patients with NSCLC. Of the known EGFR tyrosine kinase domain mutations, approximately 90% occur as deletions in exon 19 or as point mutations in exon 21, the latter resulting in arginine replacing leucine at codon 858 (L858R). The L858R activating mutation in exon 21 accounts for approximately 25-45% of EGFR-mutant NSCLC. EGFR tyrosine kinase inhibitors, or TKIs, have been developed and provide significant clinical benefit. However, patients ultimately develop resistance, often by acquisition of a secondary resistance mutation in EGFR. T790M is the most prevalent resistance mutation after first- and second-generation EGFR TKIs including gefitinib, erlotinib, afatinib, and dacomitinib. A third-generation covalent EGFR inhibitor, osimertinib, can overcome this resistance mechanism and is now approved in the first-line setting, but acquired resistance remains an issue. Patients who progress after osimertinib lack effective treatment options and the EGFR C797S mutation is the most common on-target resistance mechanism.

CFT8919 is a mutant-selective degrader targeting EGFR L858R, which remains active in the setting of resistant secondary mutations (T790M and/or C797S). We believe there may be an opportunity for CFT8919 as a component of first-line therapy, where we hope to achieve deeper and more durable responses due to the advantages of a degrader over a standard

protein inhibitor. Further, since 30-40% of mutant EGFR NSCLC patients develop brain metastases, penetration of the central nervous system sufficient to drive therapeutic effect in this compartment was a key factor in our selection of CFT8919 as our development candidate.

### Non-Small-Cell Lung Cancer

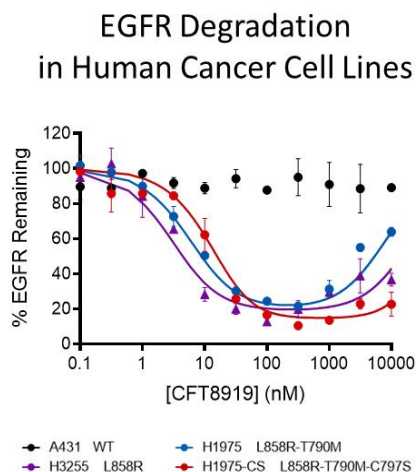
According to the National Cancer Institute, approximately 195,000 patients in the United States were diagnosed with NSCLC in 2022 and between 10 and 15% of these patients have mutant EGFR, or mEGFR. The EGFR mutation is particularly common in NSCLC patients of Asian heritage. In China, where approximately 693,000 patients are diagnosed with NSCLC annually, approximately 50% of diagnoses are driven by the EGFR mutation. Furthermore, 30 to 40% of mEGFR patients develop brain metastases.

The EGFR L858R mutation is the second most common activating EGFR mutation, found in approximately 40 percent of EGFR diagnoses in the United States and China. When treated with standard of care EGFR inhibitors, patients with EGFR L858R mutations have worse outcomes with therapy compared to patients who exhibit an exon19 deletion. When using osimertinib in the front-line setting in patients with EGFR L858R, the median PFS is 14.4 months compared to 21.4 months for patients with an exon19 deletion. The most EGFR-mediated resistance mechanism to osimertinib in this patient population is the C797S mutation. This shorter median PFS rate and resistance demonstrates the unmet medical need for the L858R patient population.

### Preclinical Development

We have conducted preclinical experiments to characterize the activity profile of our EGFR degraders and demonstrated that CFT8919 is a potent and highly selective orally bioavailable degrader of EGFR L858R with broad coverage of on-target resistance mutations as well as intracranial activity.

In human cancer cell lines *in vitro*, we have observed that CFT8919 induced potent degradation of EGFR L858R at low nanomolar concentrations while no degradation of wild type is induced up to 10  $\mu$ M. Importantly, CFT8919 retained its activity in the presence of secondary resistance mutations such as T790M and T790M-C797S. This is reflected in the graphic below.



Further, we have evaluated CFT8919 against a broad panel of EGFR resistance mutations in Ba/F3 cell models *in vitro*. Cellular growth inhibition potency, GI50, was determined by measuring the effect of various concentrations on the proliferation of Ba/F3 cells transformed by various EGFR mutations over 72 hours. As depicted in the table below,

CFT8919 demonstrated equipotent anti-proliferation activity against a large panel of EGFR secondary mutations that cause acquired resistance to the approved EGFR inhibitors such as osimertinib and erlotinib, compared to L858R single mutation.

**Ba/F3 Cell Growth Inhibition Potency (GI50, nM)**

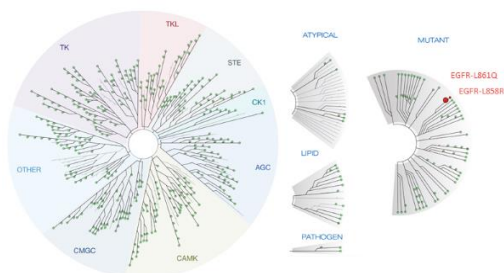
EGFR genotype		CFT8919	Osimertinib 3 <sup>rd</sup> gen	Erlotinib 1 <sup>st</sup> gen
Selectivity	wild-type	486	12	200
	1L			
	L858R	16	3	8
	L858R-T790M	16	6	5951
	2L			
	L858R-C797S	7	2753	not determined
	L858R-L718Q	23	1206	1033
	L858R-L792H	8	314	142
	3L			
	L858R-T790M-C797S	8	2671	6605
L858R-T790M-L718Q	36	1280	>10,000	
L858R-T790M-L792H	17	385	>10,000	

Color key: Potency fold change (FC) relative to L858R

Selectivity against wild-type		Activity against resistant mutations	
25 < FC	5 < FC < 25	FC < 5	25 < FC
FC < 5	FC < 5	FC < 5	FC < 5

Kinome profiling and global proteomics evaluation were conducted to evaluate binding and degradation selectivity of CFT8919, and no significant off-target activity of CFT8919 was identified. Kinome selectivity was determined using the DiscoveryX KINOMEScan assay testing 468 kinases, as shown below in the graph on the left. No wild type kinases showed binding at the 50% cutoff when CFT8919 tested at a single concentration of 100nM. The only kinases that CFT8919 exhibited significant binding were the on-target exon21 EGFR activating mutants, L858R, and L861Q. In addition, we have evaluated proteome-wide degradation selectivity by utilizing mass spectrometry to quantify cellular protein levels following 6 hours of 300 nM CFT8919 treatment in A431 EGFR-WT and H1975 EGFR-L858R-T790M cell lines *in vitro*. As depicted below in the table on the right, measurement of over 8000 proteins showed that EGFR-L858R-T790M and CCND1 are the only proteins with >50% protein level decrease induced by CFT8919 treatment, demonstrating its highly selective degradation profile. We believe that CCND1 protein loss was induced by the biological effect of EGFR suppression rather than direct degradation since this change was also observed in osimertinib EGFR inhibitor treatment.

**Kinome Binding Specificity**



**Global Proteomic Evaluation**

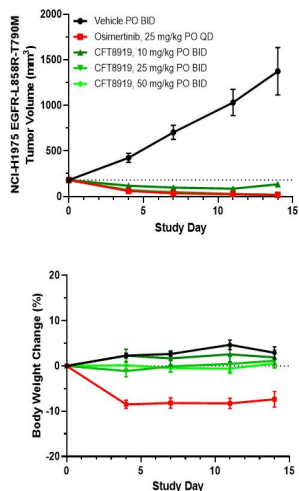
Cell line	EGFR genotype	# of proteins detected	# of proteins with >50% protein level decrease*
A431	Wild-type	9190	0
H1975	L858R-T790M	8853	2 (EGFR, CCND1)

\*p-value < 0.001

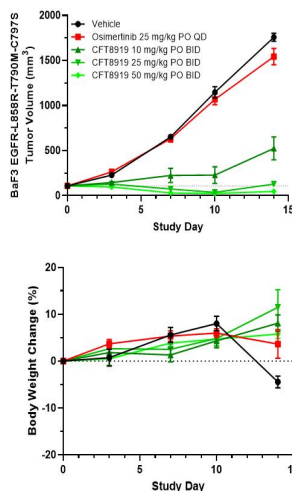


*In vivo* activity of CFT8919 was assessed in H1975 EGFR-L858R-T790M xenograft (1<sup>st</sup> generation TKI resistant) and BaF3 EGFR-L858R-T790M-C797S (osimertinib resistant) allograft models. In the H1975 xenograft model, twice daily (BID) oral administration of CFT8919 demonstrated dose-dependent activity, with tumor regression observed at doses as low as 10 mg/kg. Regression of Ba/F3 EGFR-L858R-T790M-C797S allograft tumors were achieved with CFT8919 dosed BID > 25 mg/kg, while osimertinib was inactive as expected. All doses were well tolerated, indicated by no significant body weight loss. This is reflected in the graphic below.

1st-generation EGFRi Resistant  
H1975 (L858R-T790M) Xenograft

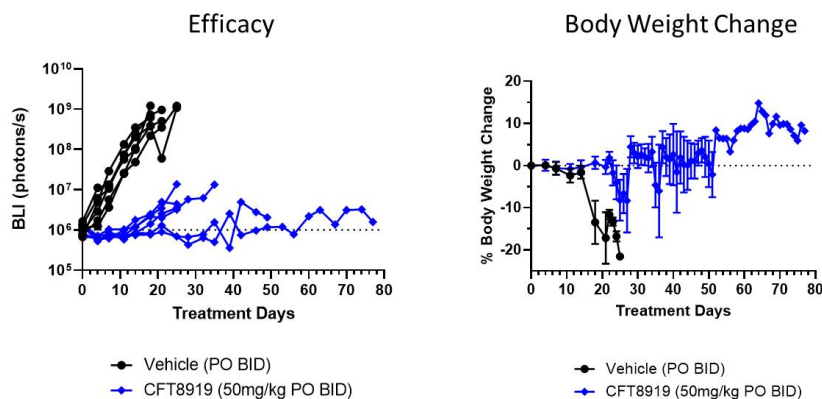


3rd-generation EGFRi Resistant  
Ba/F3 (L858R-T790M-C797S) Allograft



Intracranial activity of CFT8919 was evaluated in the H1975-LUC brain metastasis model. Female BALB/c nude mice were inoculated by intracarotid artery injection with H1975 (EGFR L858R-T790M) luciferase expressing cells. Bioluminescence imaging (BLI) was conducted to follow the tumor growth in brain. As shown in the graphic below, CFT8919 demonstrated rapid and significant reductions in tumor burden with minimal weight loss after oral dosing, indicating its potential to be active in the central nervous system.

H1975-LUC (EGFR-L858R-T790M) brain metastasis model



**Our Other Discovery Programs**

In addition to the programs discussed above, we are also progressing several other discovery-stage pipeline programs. In line with our strategy, we assess on a target-by-target basis whether our degraders would provide a compelling and differentiated approach over standard of care or other approaches to the same disease and are consistent with our focus on minimizing biology and toxicity risk, and focusing on high unmet medical need, including rare diseases. These early-stage

discovery programs include compounds that have already shown the ability to cross the blood-brain barrier in preclinical models, where appropriate. Our discovery programs are a combination of internal programs, over which we have full control and ownership, and programs in collaboration with our partners.

## **Collaborations and License Agreements**

### ***Roche Amended and Restated License Agreement***

In March 2016, we entered into a license agreement with Roche, which was amended in June 2016 and amended further in March 2017. We further amended and restated that agreement (as so amended) in December 2018. We refer to this amended and restated agreement as the Roche Agreement. Under the Roche Agreement, we agreed to collaborate with Roche in the research, development, manufacture, and commercialization of target-binding degrader medicines using our proprietary TORPEDO platform for the treatment of cancers and other indications. In November 2020, we signed a further amendment to the Roche Agreement that provides a mechanism through which we and Roche can mutually agree to terminate the Roche Agreement on a target-by-target basis by the entry into a mutual target termination agreement. Upon a termination of this nature, the Roche Agreement, as amended, provides that all rights in know-how and intellectual property in support of products that use inhibition as their mode of action, referred to as the Roche Field, will revert to Roche and all rights in respect of know-how and intellectual property in support of products that use degradation as their mode of action, referred to as the C4T Field, will revert to us. Further, this amendment states that, following the entry into a mutual target termination agreement, Roche will have rights in and responsibility for any know-how and intellectual property generated as a result of the collaboration that fits within the Roche Field, and we will have rights in and responsibility for any know-how and intellectual property generated as a result of the collaboration that fits within the C4T Field. In support of this allocation of rights, under the amendment, Roche provided us, and we provided Roche, with a perpetual, irrevocable, fully paid up, exclusive (even as to party granting the license), sublicensable (including in multiple tiers) license to the patents that are allocated to a party under the mutual target termination agreement and a perpetual, irrevocable fully paid up, non-exclusive, sublicensable (including in multiple tiers) license to the know-how that is allocable to a party under the mutual termination agreement.

In November 2020, through the entry into this amendment, we and Roche mutually agreed to terminate the Roche Agreement as to the target EGFR. As a result, Roche is now free to pursue the target EGFR in the Roche Field and we are free to pursue the target EGFR in the C4T Field, and all rights in and responsibility for know-how and intellectual property related to EGFR in the Roche Field reverted to the Roche parties, and all rights in and responsibility for know-how and intellectual property related to EGFR in the C4T Field reverted to us, with Roche assigning the patents in the C4T Field to us.

In November 2021, we and Roche mutually agreed to terminate the Roche Agreement as to the target BRAF and in July 2022, we and Roche mutually agreed to terminate the Roche Agreement as to an undisclosed target, converting each of those programs into a proprietary program for us. As a result, Roche is now free to pursue these targets in the Roche Field and we are now free to pursue these targets in the C4T Field, and all rights in and responsibility for know-how and intellectual property related to these programs in the Roche Field reverted to the Roche parties, and all rights in and responsibility for know-how and intellectual property related to in these programs in the C4T Field reverted to us, which Roche has assigned the patents for each of these programs in the C4T Field to us.

Under the terms of the Roche Agreement, we are responsible for conducting preclinical research and development activities for a number of targets selected by Roche in accordance with a target selection and replacement procedure set forth in the agreement. We are also responsible for conducting Phase 1 clinical trials for products directed to certain targets and for manufacturing activities in connection with the applicable research plans, subject to Roche's right to assume manufacturing responsibilities at pre-defined times. We and Roche each share in the costs of these research activities.

Under the Roche Agreement, we granted Roche an exclusive option to obtain an exclusive, worldwide license, with the right to sublicense through multiple tiers to develop and commercialize products directed at each target that is subject to the collaboration. Upon the exercise of its option for a particular target, Roche is responsible for the manufacture, development, and commercialization of products directed to that target, at its sole expense. However, we have the option to co-develop products directed to certain targets, in which case we would be responsible for a portion of the development costs associated with such co-developed products and eligible to receive increased royalties on sales of such co-developed products. We also have an option to co-detail products for which have exercised our co-development option. If we exercise our co-detail option, we will be responsible for a portion of the co-detailing costs. We generally have the right to opt out of these co-development and co-detailing activities.

Upon signing the Roche Agreement, we received upfront consideration of \$40.0 million from Roche. In addition, we receive annual research funding from Roche for each active research plan and we are eligible to receive additional payments upon the achievement of predetermined research and development success criteria with respect to certain targets.

If Roche exercises its option right for a target, Roche is obligated to pay an exercise fee ranging from \$7.0 million to \$20.0 million, depending on the target. For each target option exercised by Roche, we are eligible to receive milestone payments up to a range of \$260 million to \$275 million upon the achievement of certain research, development, and commercial milestones with respect to corresponding products, subject to certain reductions and exclusions based on intellectual property coverage. Roche is also required to pay us up to \$150 million per target in one-time sales-based milestone payments upon the achievement of specified levels of net sales of a product directed to such target. Finally, we are eligible to receive tiered royalties ranging from mid-single digit to mid-teen percentages on net sales of products sold by Roche pursuant to its exercise of its option rights, subject to certain reductions. For sales of products for which we exercise our co-development right, the applicable royalty rates will be increased by a low-single digit percentage.

Unless earlier terminated, the Roche Agreement expires on the date when no royalty or other payment obligations under the Roche Agreement are or will become due. We and Roche each may terminate the Roche Agreement in its entirety or on a target-by-target or product-by-product basis and, in our case, on a country-by-country basis, for the other party's uncured material breach of its obligations under the Roche Agreement or upon the other party's bankruptcy, insolvency or similar proceedings. Roche may terminate the Roche Agreement for convenience on a target-by-target, product-by-product or country-by-country basis. In the event we are acquired by a competitor of Roche, Roche has the right to require us to terminate our research, development, and co-detailing activities under the Roche Agreement, after which time we would not be eligible to receive payments for such terminated activities.

#### ***Calico License Agreement***

In March 2017, we entered into a Collaboration and License Agreement, or the Calico Agreement, with Calico, whereby we agreed to collaborate with Calico to discover, develop, and commercialize small molecule protein degraders for diseases of aging, including cancer, for a five-year research term ending in March 2022. In August 2021, we provided Calico with an option to extend the research term with respect to a certain program for up to a one-year period ending in March 2023 and, in September 2021, Calico exercised this option.

Under the Calico Agreement, we and Calico each agreed to conduct joint research activities with respect to a number of targets selected by Calico in accordance with a target selection and replacement procedure set forth in the agreement. During the research term, Calico is responsible for the costs of these research activities and has the right to approve targets for advancement to lead optimization activities to be carried out by the parties under the corresponding research plans.

Upon the completion of our research activities for each target selected by Calico for lead optimization activities, Calico is responsible for, and agrees to use commercially reasonable efforts to carry out, all further preclinical development, regulatory affairs, manufacturing, and commercialization for products directed against each such target. We refer to these products as Collaboration Products. We granted Calico an exclusive license to manufacture and commercialize Collaboration Products under certain of our intellectual property rights.

Under this agreement, Calico paid us an upfront amount of \$5.0 million and certain annual payments totaling \$5.0 million through December 31, 2020. Upon exercising its option to extend the research term with respect to a certain program ending in March 2023, Calico paid us an additional fee of \$1.0 million. Upon successful nomination of a target following a target evaluation phase and initiation of the applicable research plan, we are eligible to receive target initiation payments from Calico. For each target, we are eligible to receive research, development, and commercial milestone payments totaling up to \$132.0 million. Calico is also required to pay one-time sales-based milestone payments aggregating up to \$65.0 million upon the achievement of specified levels of net sales of a product directed to such target, subject to a reduction based on intellectual property coverage. We are also eligible to receive royalty payments on the net sales of Collaboration Products, at percentages in the mid-single digits, subject to certain reductions.

Unless terminated earlier, the Calico Agreement expires on the date when no royalty or other payment obligations under the Calico Agreement are or will become due. We and Calico each may terminate the Calico Agreement in its entirety or on a target-by-target or product-by-product basis and, in our case, on a country-by-country basis, for the other party's uncured material breach of its obligations or its bankruptcy or insolvency. Calico may terminate the Calico Agreement for convenience in its entirety or on a target-by-target or country-by-country basis, subject to reimbursement of costs and return of materials. The research term under the Calico Agreement will end in March 2023.

#### ***Biogen Collaborative Research and License Agreement***

In December 2018, we entered into a collaborative research and license agreement, or the Biogen Agreement, with Biogen, whereby we agreed to collaborate with Biogen and use our proprietary protein degrader platform to research, develop, and identify small molecule protein degraders. In February 2020, we entered into an amendment to the Biogen Agreement that provided further clarity around Biogen's ownership of target binding moieties, which are portions of molecules, and any related intellectual property that are directed at or bind to collaboration targets. This amendment further provides that

Biogen licenses to us rights to use these Biogen target binding moieties and any related intellectual property as needed in order to conduct the research and development activities contemplated under the Biogen Agreement.

Under the Biogen Agreement, we granted Biogen an exclusive license under our intellectual property, with the right to sublicense through multiple tiers, (a) for the purpose of performing candidate development activities in accordance with research and development plans agreed upon by the parties and (b) for the purpose of exploiting all degraders and products for any use in the world.

Under the terms of the Biogen Agreement, we are responsible for conducting research and development activities for a number of targets selected by Biogen in accordance with a target selection and replacement procedure set forth in the agreement. We are required to provide all resources necessary to perform candidate development activities, perform those activities with reasonable care and skill and in accordance with applicable law and the Biogen Agreement and use diligent efforts to complete the activities as set forth in the applicable development plan and deliver to Biogen a certain number of degraders directed to each target that meet a range of pre-defined criteria. We and Biogen are also responsible for research activities designed to inform Biogen's target selection process, for which Biogen will pay for its own costs and will reimburse our costs up to a certain amount. The research term under the Biogen Agreement will end in June 2023.

Upon Biogen's commencement of the IND-enabling study for a degrader directed towards each target selected by Biogen, Biogen is responsible for, and agrees to use commercially reasonable efforts to carry out, all further development, regulatory affairs, manufacturing, and commercialization for at least one product directed against each such target in certain territories.

Upon execution of the Biogen Agreement, Biogen paid us an upfront payment of \$45.0 million as prepayment for candidate development activities. Upon Biogen's receipt of degraders directed to each target that satisfy pre-defined criteria, we are eligible to receive payments ranging from \$2.0 million to \$5.0 million per target. Upon Biogen's commencement of the first IND-enabling study for a development candidate directed towards each target, Biogen is required to pay us \$8.0 million. For each target, Biogen is required to pay us (a) development and commercialization milestone payments totaling up to \$35.0 million and (b) sales milestone payments totaling up to \$26.0 million for the achievement of certain amounts of net sales of all products directed to such target, each subject to certain reductions. The total development, commercialization, and sales milestone payments will increase if Biogen extends the collaboration term and elects additional targets. In addition, Biogen is required to pay us royalties on a product-by-product and country-by-country basis on the net sales of each product, at percentages in the mid-single digits, subject to certain reductions.

Unless earlier terminated, the Biogen Agreement expires on the date of the last product-by-product and country-by-country basis upon the expiration of the last-to-expire valid claim of a patent right covering the composition of matter of method of use in the approved label of the applicable product in the applicable country. We and Biogen each may terminate the Biogen Agreement (a) with respect to one or more development candidates, products or collaboration targets or, only in the case of Biogen, the entire agreement, for the other party's uncured material breach of its obligations and (b) in its entirety upon the other party's bankruptcy, insolvency or similar proceedings. Biogen may also terminate the Biogen Agreement in its entirety or with respect to one or more development candidates, products or collaboration targets for convenience.

## **Competition**

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition, and a strong emphasis on intellectual property and proprietary products. While we believe that our technology, expertise, scientific knowledge, and intellectual property estate provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical, and biotechnology companies, academic institutions, governmental agencies, and public and private research institutions that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing, and commercialization. Not only must we compete with other companies that are focused on protein degradation, but any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future. Moreover, our industry is characterized by the existence of large numbers of patents and frequent allegations of patent infringement.

Our focus is on the discovery and development of protein degradation therapies using our TORPEDO platform. Other companies developing chimeric small molecules for protein degradation include, without limitation, Arvinas, Inc., BioTheryX, Inc., Captor Therapeutics, Inc., Cullgen Inc., Foghorn Therapeutics, Inc., Frontier Medicines Corporation, Haisco Pharmaceutical Group, Kymera Therapeutics, Inc., Monte Rosa Therapeutics, Inc., Nurix Therapeutics, Inc., PhoreMost Ltd., Plexium, Inc., Proteovant Therapeutics, Inc., Salarius Pharmaceuticals, Inc., Seed Therapeutics, Inc., and Vividion Therapeutics, Inc. (a subsidiary of Bayer AG). Further, several large pharmaceutical companies have disclosed preclinical investments in this field including Amgen, Astellas Pharma Inc., AstraZeneca plc, Bristol-Myers Squibb Company (and its subsidiary Celgene Corporation), GlaxoSmithKline plc, Genentech, Inc., and Novartis International AG.

In addition to competition from other protein degradation therapies, any products that we develop may also face competition from other types of therapies, such as small molecule, antibody, T cell or gene therapies. For example, we understand that Adaptimmune Limited, Foghorn Therapeutics, Inc., and GlaxoSmithKline plc are pursuing the development of therapies for patients with synovial sarcoma.

Our lead product candidates target oncologic indications. The most common methods of treating patients in oncologic indications are surgery, radiation, and drug therapy, including chemotherapy, hormone therapy, cellular therapy, and targeted drug therapy. There are a variety of available drug therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy. Some of the currently approved drug therapies are branded and subject to patent protection and others are available on a generic basis. Many of these approved drugs are therapies and are widely accepted by physicians, patients, and third-party payors. In general, although there has been considerable progress over the past few decades in the treatment of cancer and the currently marketed therapies provide benefits to many patients, these therapies are all limited to some extent in their efficacy and frequency of adverse events, and none of them are successful in treating all patients. As a result, the level of morbidity and mortality from cancer remains high.

In addition to currently marketed drugs, there are also several product candidates in preclinical development for the treatment of oncologic indications. These products in development may provide efficacy, safety, convenience, and other benefits that are not provided by currently marketed therapies. As a result, they may provide significant competition for any of our product candidates for which we obtain market approval.

If any of our product candidates are approved for the indications for which we expect to conduct clinical trials, they will compete with the foregoing therapies and currently marketed drugs, as well as any drugs potentially in development. It is also possible that we will face competition from other biologic or pharmaceutical approaches, as well as from other types of therapies.

Many of our current or potential competitors, either alone or with their collaboration partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals, and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel, and establishing clinical trial sites, and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel, and establishing clinical trial sites, and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic products. There are generic products currently on the market for certain of the indications that we are pursuing, and additional products are expected to become available on a generic basis over the coming years. If our product candidates are approved, we expect that they will be priced at a significant premium over competitive generic products.

The key competitive factors affecting the success of all our programs, if approved, are likely to be their efficacy, safety, convenience, price, level of generic competition, and availability of reimbursement.

### **Manufacturing**

We do not own or operate and currently have no plans to establish any manufacturing facilities. We rely on and expect to continue to rely on third-party contract manufacturing organizations, or CMOs, for both drug substance and finished drug product.

We currently obtain our supplies from these manufacturers on a purchase order basis and do not have long-term committed supply arrangements with respect to our product candidates and other materials. Should any of these manufacturers become unavailable to us for any reason, we believe that there are a number of potential replacements, although we may incur some delay in identifying and qualifying such replacements. For additional information, see the section titled “Risk Factors—Risks Related to Dependence on Third Parties—Manufacturing pharmaceutical products is complex and subject to product delays or loss for a variety of reasons. We contract with third parties for the manufacture of our product candidates for preclinical testing and clinical trials and expect to continue to do so for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or that we will not have

*the quantities we desire or require at an acceptable cost or quality or at the right time, which could delay, prevent or impair our development or commercialization efforts.”*

All of our drug candidates are organic compounds of low molecular weight, which are often referred to in the biopharmaceutical community as small molecules, but our BiDAC degraders tend to be larger than traditional small molecule therapeutics. We have selected these compounds not only on the basis of their potential clinical activity and tolerability, but also for their relative ease of synthesis and reasonable cost of goods. In particular, CFT7455 and CFT8634 are manufactured using reliable and reproducible synthetic processes from readily available starting materials. The chemistry is amenable to scale up and does not require unusual equipment in the manufacturing process. We expect to continue to develop drug candidates that can be produced cost effectively at contract manufacturing facilities.

### **Commercialization Plans**

We have not yet established our own commercial organization or distribution capabilities because our product candidates are still in clinical development, with our three most advanced programs in the clinic and our fourth most advanced program expected to enter the clinic in 2023. We have retained full commercialization rights for all of our programs in development other than those subject to our collaboration agreements. Prior to any of our product candidates receiving marketing approval, at an appropriate time, we will need to develop a plan to commercialize them in the United States and other key markets. We currently anticipate that we would build our own focused, specialized sales, and marketing organization to support the commercialization in the United States of product candidates for which we receive marketing approval and that can be commercialized with such capabilities. We expect to utilize a variety of types of collaboration, co-promotion, distribution, and other marketing arrangements with one or more third parties to commercialize our product candidates in markets outside the United States or for situations in which a larger sales and marketing organization is required.

As product candidates advance through our pipeline, our commercial plans may change. Some of our research programs target potentially larger indications. Data, the size of the development programs, the size of the target market, the size of a commercial infrastructure, and manufacturing needs may all influence our strategies in the United States, Europe, and the rest of the world.

### **Intellectual Property**

Our commercial success depends in part upon our ability to secure and maintain patent and other proprietary protection for our protein degradation technologies, including our TORPEDO platform, our solely-owned product candidates, our product candidates co-owned with Roche and know-how related to our business. To protect our core technology and products, we will need to successfully prosecute, defend and, if necessary, enforce our intellectual property rights, including, in particular, our patent rights, preserve the confidentiality of our trade secrets and operate without infringing valid and enforceable intellectual property rights of others. For our product candidates, we generally intend to pursue patent protection covering compositions of matter, pharmaceutical compositions, methods of use, including combination therapies, processes of manufacture and process intermediates, where relevant. We continually assess and refine our intellectual property strategies as we develop new technologies and product candidates. We currently plan to file additional patent applications based on our intellectual property strategies, where appropriate, including where we seek to adapt to competition or to improve our business opportunities.

The patent positions for biopharmaceutical companies like us are generally uncertain and can involve complex legal, scientific, and factual issues. Further, the laws governing the protection of intellectual property may change over time due to the issuance of new judicial decisions or the passage of new laws, rules or regulations. In addition, the coverage claimed in a patent application can be significantly reduced before a patent is issued and its scope can be reinterpreted and challenged even after issuance. As a result, we cannot guarantee that any of our product candidates will be protected or remain protectable by valid, enforceable patents. We also cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient proprietary protection from competitors. Any patents that we hold may be challenged, circumvented or invalidated by third parties.

The exclusivity terms of our patents depend upon the laws of the countries in which they are obtained. In the countries in which we currently file, the patent term is 20 years from the earliest date of filing of a non-provisional patent application. The term of a United States patent may be extended to compensate for the time required to obtain regulatory approval to sell a drug (referred to as a patent term extension) or by delays encountered during patent prosecution that are caused by the United States Patent and Trademark Office (referred to as patent term adjustment). For example, the Hatch-Waxman Act permits a patent term extension for FDA-approved new chemical entity drugs of up to five years beyond the ordinary expiration date of one patent that covers the approved drug or its use. The length of the patent term extension is related to the length of time the drug is under regulatory review and diligence during the review process. Patent term extensions in

the United States cannot extend the term of a patent beyond a total of 14 years from the date of product approval and only one patent covering an approved drug, or its method of use may be extended. A similar kind of patent extension, referred to as a Supplementary Protection Certificate, is available in Europe. Legal frameworks may also be available in certain other jurisdictions to extend the term of a patent. We currently intend to seek patent term extensions for our products on any of our issued patents in any jurisdiction where we have a qualifying patent and the extension is available; however, there is no guarantee that the applicable regulatory authorities, including the FDA in the United States, will agree with our assessment of whether extensions of this nature should be granted and, even if granted, the length of these extensions. Further, even if any of our patents are extended or adjusted, those patents, including the extended or adjusted portion of those patents, may be held invalid or unenforceable by a court of final jurisdiction in the United States or a foreign country.

### ***Patents and Patent Applications***

As of December 31, 2022, in total, we owned ten issued United States patents, more than 25 United States patent applications (which include provisional and United States utility applications), ten patent applications filed under the Patent Cooperation Treaty, or PCT, and over one hundred fifty patent applications that are pending in foreign countries.

Our patent portfolio is generally organized into two categories: platform patent filings designed to cover inventions generated through our proprietary TORPEDO platform and protein target-specific degrader filings, each of which categories is described in more detail below.

### ***TORPEDO Platform Portfolio***

We solely own our platform patent estate, which has been designed using our proprietary TORPEDO platform. As of December 31, 2022, our platform patent portfolio included nine issued United States patents, 15 pending United States patent applications, two PCT patent applications, and forty pending foreign patent applications. This patent portfolio covers a variety of our toolbox ligands that bind to the Cereblon E3 ubiquitin ligase, or CRBN, either alone, as part of a MonoDAC molecule, or as part of a BiDAC molecule that includes a protein ligand to a disease-modifying protein target.

Specifically, this platform portfolio consists of 17 patent families covering the TORPEDO platform with composition of matter claims directed to various classes of CRBN ligands and degraders derived therefrom, as well as claims to associated methods of use, pharmaceutical compositions, and processes of manufacture. Patent applications for several of these patent families have been filed in the United States, China, and Europe. Patents in these families, if issued and maintained, will expire between 2037 and 2043, without taking into account potential patent term extensions or adjustments.

### ***Products and Target Portfolio***

Our patent applications directed to target-specific degraders, including our product candidates, are focused on composition of matter, pharmaceutical composition, method of use, and process of manufacture claims covering novel compounds designed to degrade disease-causing proteins. As of December 31, 2022, we owned one issued United States patent, 12 pending United States patent applications, eight PCT patent applications, and more than 110 foreign patent applications covering our degrader and product candidates.

Specifically, as of December 31, 2022, we owned four patent families (one United States patent, four United States patent applications, one PCT patent application, and 38 foreign patent applications) presenting composition of matter and pharmaceutical composition claims to compounds that cause the degradation of the IKZF1/3 protein target, as well as associated methods of use to treat cancer and processes of manufacture. Three of these patent families include claims directed to compositions of matter generally and specifically covering CFT7455, one of our lead product candidates and associated methods of use, which if issued and maintained through the payment of all required fees, will expire in 2040, 2041, and 2043, respectively, without regard to any possible patent term extensions or adjustments. The fourth patent family covering our IKZF1/3 degraders is directed to a separate genus than that covered in the previous three families and, if granted and maintained through the payment of all required fees, will expire in 2039, without regard to any possible patent term extensions or adjustments.

As of December 31, 2022, we owned three United States patent applications, one PCT patent application, and 23 foreign patent applications with claims directed to compositions of matter covering our BRD9 degraders, including our CFT8634 product candidate, and associated pharmaceutical compositions, methods of use, and processes of manufacture. United States and foreign patents claiming priority to these patent applications, if granted and maintained through the payment of all required fees, will expire in 2041 and 2042, without regard to any possible patent term extensions or adjustments.

As of December 31, 2022, we owned three patent families (one United States patent application, one PCT patent application, and eight foreign patent applications) with claims directed to compositions of matter covering our BRAF degraders, and associated methods of use, pharmaceutical compositions, and processes of manufacture. Two of these patent families include claims directed to compositions of matter generally and specifically covering CFT1946, our lead BRAF product candidate, and associated methods of use, and United States and foreign patents claiming priority to these patent

applications, if granted and maintained through payment of all required fees, will expire in 2042 and 2043, respectively, without regard to any possible patent term extensions or adjustments. The third patent family covering our BRAF degraders is directed to a separate genus than that covered by the previous two families, and United States and foreign patents claiming priority to these patent applications, if granted and maintained through the payment of all required fees, will expire between in 2041, without regard to any possible patent term extensions or adjustments.

As of December 31, 2022, we owned one United States patent application, one PCT patent application, and 36 foreign patent applications, with claims directed to compositions of matter covering our EGFR degraders, including our CFT8919 product candidate, and associated methods of use, pharmaceutical compositions, and processes of manufacture. United States and foreign patents claiming priority to these patent application, if granted and maintained through the payment of all required fees, will expire between 2040 and 2042, without regard to any possible patent term extensions or adjustments.

As of December 31, 2022, we owned one PCT patent application with claims directed to compositions of matter covering our RET degraders and associated methods of use, pharmaceutical compositions, and processes of manufacture. United States and foreign patents claiming priority to this patent application, if granted and maintained through the payment of all required fees, will expire in 2041, without regard to any possible patent term extensions or adjustments.

As of December 31, 2022, we owned three United States patent applications, three PCT patent applications, and nine foreign patent applications with claims directed to compositions of matter covering degraders to undisclosed targets and associated methods of use, pharmaceutical compositions, and processes of manufacture. United States and foreign patents claiming priority to these patent applications, if granted and maintained through the payment of all required fees, will expire in between 2040 and 2043, without regard to any possible patent term extensions or adjustments.

#### ***Collaboration Patent Applications Co-owned with Roche***

As of December 31, 2022 (giving effect to the assignment of rights in patents related to the undisclosed target from Roche to us in July 2022, as described above), we do not co-own any patent applications or patents with Roche. If new patent applications relating to ongoing collaboration activities are filed in the future, our rights to any such future patent applications will be governed by the Roche Agreement, which is described above.

#### ***Target Platform Collaborations***

We work with three strategic partners to expand our platform potential: Roche, Calico, and Biogen. Under the agreements with each of these partners, we generally assign our solely or co-invented patent rights in development candidates to the applicable partner in exchange for financial benefits in the products under development under those agreements

#### ***Trade Secrets***

We also rely on trade secrets, technical know-how and continuing innovation to develop and maintain our competitive advantage. Under the agreements we enter into with our employees and consultants who are identified on any company-owned patent applications assign any rights they may have in any such patent application to us. We also rely on confidentiality or other agreements with our employees, consultants, and other advisors to protect our proprietary information. Our policy is to require third parties that receive material confidential information to enter into confidentiality or other agreements with us that contain appropriate protections for our confidential and trade secret information.

#### ***Trademarks***

We own various registered and unregistered trademarks and service marks in the United States and overseas, including C4 THERAPEUTICS, our housemark logo, the name of our TORPEDO platform, and the names of our BIDAC degraders and MONODAC degraders.

#### **Government Regulation**

The FDA and comparable regulatory agencies in state and local jurisdictions, and in foreign countries impose substantial requirements upon the clinical development, manufacture, and marketing of pharmaceutical products. These agencies and other federal, state and local entities regulate research and development activities, and the testing, manufacture, quality control, safety, effectiveness, labeling, storage, packaging, recordkeeping, tracking, approval, import, export, distribution, advertising, and promotion of our products.

#### ***United States Government Regulation of Drug Products***

In the United States, the FDA regulates drugs under the Federal Food, Drug and Cosmetic Act, or the FDCA, and its implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes, and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable United States requirements at any time during the product development process, approval process or after approval may subject an applicant to a variety of administrative or judicial sanctions, such as the



FDA's refusal to approve a pending NDA, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties.

The process required by the FDA before product candidates may be marketed in the United States generally involves the following:

- nonclinical laboratory and animal tests that must be conducted in accordance with GLP;
- submission to the FDA of an investigational new drug, or IND, application, which must become effective before clinical trials may begin;
- approval by an independent institutional review board, or IRB, for each clinical site or centrally before each trial may be initiated;
- adequate and well controlled human clinical trials to establish the safety and efficacy of the proposed product candidate for its intended use, performed in accordance with good clinical practices, or GCP;
- submission to the FDA of an NDA and payment of user fees;
- satisfactory completion of an FDA advisory committee review, if applicable;
- pre-approval inspection of manufacturing facilities and selected clinical investigators for their compliance with current good manufacturing practices, or cGMP, and GCP;
- satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCP and the integrity of the clinical data; and
- FDA review and approval of an NDA to permit commercial marketing for particular indications for use.

The testing and approval process requires substantial time, effort, and financial resources.

### ***Preclinical Studies***

Preclinical studies include laboratory evaluation of drug substance chemistry, pharmacology, toxicity, and drug product formulation, as well as animal studies to assess potential safety and efficacy. Prior to commencing the first clinical trial with a product candidate, a sponsor must submit the results of the preclinical tests and preclinical literature, together with manufacturing information, analytical data, and any available clinical data or literature, among other required information, to the FDA as part of an IND. Some preclinical studies may continue even after the IND is submitted. 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 conduct of the clinical trial and imposes a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in FDA authorization to commence a clinical trial.

### ***Clinical Trials***

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development, as well as amendments to previously submitted clinical trials. Further, an independent IRB for each institution participating in the clinical trial must review and approve the plan for any clinical trial, its informed consent form, and other communications to study subjects before the clinical trial commences at that site. The IRB must continue to oversee the clinical trial while it is being conducted, including any changes to the study plans.

Regulatory authorities, an IRB or the sponsor may suspend or discontinue a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk, the clinical trial is not being conducted in accordance with the FDA's or the IRB's requirements or if the drug has been associated with unexpected serious harm to subjects. Some studies also include a data safety monitoring board, which receives special access to unblinded data during the clinical trial and may advise the sponsor to 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.

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

- Phase 1—Studies are initially conducted to test the product candidate for safety, dosage tolerance, structure-activity relationships, mechanism of action, absorption, metabolism, distribution, and excretion in healthy volunteers or subjects with the target disease or condition. If possible, Phase 1 clinical trials may also be used to gain an initial indication of product effectiveness.

- Phase 2—Controlled studies are conducted with groups of subjects with a specified disease or condition to provide enough data to evaluate the preliminary efficacy, optimal dosages and dosing schedule, and expanded evidence of safety. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expansive Phase 3 clinical trials.
- Phase 3—These clinical trials are generally undertaken in larger subject populations to provide statistically significant evidence of clinical efficacy and to further test for safety in an expanded subject population at multiple clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the product and provide an adequate basis for product labeling. These clinical trials may be done at trial sites outside the United States as long as the global sites are also representative of the U.S. population and the conduct of the study at global sites comports with FDA regulations and guidance, such as compliance with GCPs.

Typically, clinical trials are designed in consultation with the FDA or foreign regulatory authorities during these development phases. The indications under development can influence the study designs employed during the conduct of clinical trials, such as for a first-line cancer treatment indication which may require head-to-head data demonstrating clinical superiority or non-inferiority to currently available therapies. The timeline for first-line cancer indication development programs may also be longer than for indications sought in third-line treatment or beyond due to a desire for regulatory authorities to expedite access to later-line treatments for those whose cancer has progressed despite available and earlier-line treatments. As such, many new oncology products initially seek an indication in treatment for third-line treatment, a smaller available treatment population in any oncology indication, and any later approvals sought for those products in earlier lines of treatment that target a larger treatment population might require the conduct of additional clinical trials.

The FDA has implemented initiatives that may affect the development of oncology product candidates. For example, Project Optimus, which was launched in 2021, is an initiative to reform the dose selection and dose optimization paradigm across oncology drug development to emphasize selection of a dose or doses that maximize not only the efficacy of a drug but also its safety and tolerability. Project Optimus will require that developers of oncology drugs implement strategies in ongoing programs to leverage nonclinical and clinical data in dose selection, including the potential need to conduct randomized evaluations of a range of doses in trials, and require that these studies take place as early as possible in the development program.

In addition, in March 2022, the FDA released a final guidance entitled “Expansion Cohorts: Use in First-In-Human Clinical Trials to Expedite Development of Oncology Drugs and Biologics,” which outlines how drug developers can utilize an adaptive trial design commonly referred to as a seamless trial design in early stages of oncology drug development (i.e., the first-in-human clinical trial) to compress the traditional three phases of trials into one continuous trial called an expansion cohort trial. Information to support the design of individual expansion cohorts are included in IND applications and assessed by the FDA. Expansion cohort trials can potentially bring efficiency to drug development and reduce developmental costs and time.

The FDA may require, or companies may pursue, additional clinical trials after a product is approved. These so-called Phase 4 trials may be made a condition to be satisfied after approval. The results of Phase 4 trials can confirm the effectiveness of a product candidate and can provide important safety information.

Clinical trials must be conducted under the supervision of qualified investigators in accordance with GCP requirements, which include the requirements that all research subjects provide their informed consent in writing for their participation in any clinical trial and the review and approval of the study by an IRB. Investigators must also provide information to the clinical trial sponsors to allow the sponsors to make specified financial disclosures to the FDA. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, the trial procedures, the parameters to be used in monitoring safety and the efficacy criteria to be evaluated and a statistical analysis plan. Information about some clinical trials, including a description of the trial and trial results, must be submitted within specific timeframes to the NIH for public dissemination on their website. Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur.

The manufacture of investigational drugs for the conduct of human clinical trials is subject to cGMP requirements. Investigational drugs and active pharmaceutical ingredients imported into the United States are also subject to regulation by the FDA relating to their labeling and distribution. Further, the export of investigational drug products outside of the United States is subject to regulatory requirements of the receiving country, as well as U.S. export requirements under the FDCA. Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and the IRB, and more frequently if serious adverse effects occur.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the product candidate, as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process

must be capable of consistently producing quality batches of the product candidate and, among other things, must develop methods for testing the identity, strength, quality, and purity of the final product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

### ***Special FDA Expedited Review and Approval Programs***

The FDA has various programs, including fast track designation, breakthrough therapy designation, orphan drug designation, accelerated approval, and priority review, which are intended to expedite or simplify the process for the development and FDA review of drugs that are intended for the treatment of serious or life-threatening diseases or conditions and demonstrate the potential to address unmet medical needs. The purpose of these programs is to provide important new drugs to patients earlier than under standard FDA review procedures.

Under the fast track program, the sponsor of a new drug candidate may request that FDA designate the drug candidate for a specific indication as a fast track drug concurrent with, or after, the filing of the IND for the drug candidate. To be eligible for a fast track designation, the FDA must determine, based on the request of a sponsor, that a product is intended to treat a serious or life threatening disease or condition and demonstrates the potential to address an unmet medical need. The FDA will determine that a product will fill an unmet medical need if it will provide a therapy where none exists or provide a therapy that may be potentially superior to existing therapy based on efficacy or safety factors. Fast track designation provides additional opportunities for interaction with the FDA's review team and may allow for rolling review of NDA components before the completed 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. However, the FDA's time period goal for reviewing an application does not begin until the last section of the NDA is submitted. The FDA may decide to rescind the fast track designation if it determines that the qualifying criteria no longer apply.

In addition, a sponsor can request breakthrough therapy designation for a drug if it is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Drugs designated as breakthrough therapies are eligible for intensive guidance from the FDA on an efficient drug development program, organizational commitment to the development and review of the product, including involvement of senior managers, and, like fast track products, are also eligible for rolling review of the NDA. Both fast track and breakthrough therapy products may be eligible for accelerated approval and/or priority review, if relevant criteria are met.

Under the Orphan Drug Act, the FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition (generally meaning that it affects fewer than 200,000 individuals in the United States or more in cases in which there is no reasonable expectation that the cost of developing and making a drug product available in the United States for treatment of the disease or condition will be recovered from sales of the product). A company must request orphan product designation before submitting an NDA. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product with orphan status receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will be receiving orphan product exclusivity. Orphan product exclusivity means that the FDA may not approve any other applications for the same product for the same indication for seven years, except in certain limited circumstances. If a drug or drug product designated as an orphan product ultimately receives marketing approval for an indication broader than what was designated in its orphan product application, it may not be entitled to exclusivity. Orphan exclusivity will not bar approval of another product under certain circumstances, including if a subsequent product with the same active ingredient for the same indication is shown to be clinically superior to the approved product on the basis of greater efficacy or safety or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand. Further, the FDA may approve more than one product for the same orphan indication or disease as long as the products contain different active ingredients. Moreover, competitors may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity.

Under the FDA's accelerated approval regulations, the FDA may approve a drug for a serious or life threatening illness that provides meaningful therapeutic benefit to patients over existing treatments based upon a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, 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. A drug candidate approved on this basis is subject to rigorous post marketing compliance requirements,

including the completion of Phase 4 or post approval clinical trials to confirm the effect on the clinical endpoint. Under the Food and Drug Omnibus Reform Act of 2022, or FDORA, the FDA is now permitted to require, as appropriate, that these trials be underway prior to approval or within a specific time period after the date of approval for a product granted accelerated approval. Under FDORA, the FDA has increased authority for expedited procedures to withdraw approval of a drug or indication approved under accelerated approval if, for example, the confirmatory trial fails to verify the predicted clinical benefit of the product. All promotional materials for drug candidates approved under accelerated approval regulations are subject to prior review by the FDA unless the sponsor is otherwise informed by the FDA.

Once an NDA is submitted for a product intended to treat a serious condition, the FDA may assign a priority review designation if FDA determines that the product, if approved, would provide a significant improvement in safety or effectiveness. A priority review means that the goal for the FDA to review an application is six months, rather than the standard review of ten months under the Prescription Drug User Fee Act, or PDUFA, guidelines. Under the current PDUFA performance goals, these six- and ten-month review periods are measured from the 60-day filing date rather than the receipt date for NDAs for new molecular entities, which typically adds approximately two months to the timeline for review from the date of submission.

Even if a product 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. In addition, the manufacturer of an investigational drug for a serious or life-threatening disease is required to make available, such as by posting on its website, its policy on responding to requests for expanded access. Furthermore, fast track designation, breakthrough therapy designation, accelerated approval, and priority review do not change the standards for approval and may not ultimately expedite the development or approval process.

#### ***NDA Submission and Review by the FDA***

Assuming successful completion of the required clinical and preclinical testing, among other items, the results of product development, including chemistry, manufacture and controls, nonclinical studies and clinical trials are submitted to the FDA, along with proposed labeling, as part of an NDA. The submission of an NDA requires payment of a substantial user fee to the FDA. These user fees must be filed at the time of the first submission of the application, even if the application is being submitted on a rolling basis. Fee waivers or reductions are available in some circumstances. One basis for a waiver of the application user fee is if the applicant employs fewer than 500 employees, including employees of affiliates, the applicant does not have an approved marketing application for a product that has been introduced or delivered for introduction into interstate commerce and the applicant, including its affiliates, is submitting its first marketing application.

In addition, under the Pediatric Research Equity Act, or PREA, an NDA or supplement to an NDA for a new active ingredient, indication, dosage form, dosage regimen or route of administration must contain data that are adequate to assess the safety and efficacy of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. Unless otherwise required by regulation, PREA does not apply to a drug for an indication for which orphan drug designation has been granted, except that PREA will apply to an original NDA for a new active ingredient that is orphan-designated if the drug is a molecularly targeted cancer product intended for the treatment of an adult cancer and is directed at a molecular target that FDA determines to be substantially relevant to the growth or progression of a pediatric cancer. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults or full or partial waivers from the pediatric data requirements.

The FDCA also provides incentives for sponsors to conduct studies of drugs in pediatric populations. A drug may be eligible for pediatric exclusivity if a sponsor voluntarily completes a pediatric study that fairly responds to an FDA-issued Written Request. If granted, pediatric exclusivity adds six months to existing regulatory exclusivity periods and patent terms for all approved drug products that contain the active moiety for which pediatric exclusivity was granted.

The FDA must refer applications for drugs that contain active ingredients, including any ester or salt of the active ingredients, which have not previously been approved by the FDA to an advisory committee or provide in an action letter a summary of the reasons for not referring it to an advisory committee. The FDA may also refer drugs which present difficult questions of safety, purity or potency to an advisory committee. An advisory committee is typically a panel that includes clinicians and other experts who review, evaluate, and make 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.

The FDA reviews applications to determine, among other things, whether a product is safe and effective for its intended use and whether the manufacturing controls are adequate to assure and preserve the product's identity, strength, quality, and purity. Before approving an NDA, the FDA will 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, including contract manufacturers and subcontracts, are in compliance with cGMP requirements and adequate to assure consistent

production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical trial sites to assure compliance with GCPs.

Once the FDA receives an application, it has 60 days to review the NDA to determine if it is substantially complete to permit a substantive review, before it accepts the application for filing. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. Under the goals and policies agreed to by the FDA under PDUFA, the FDA has set the review goal of 10 months from the 60-day filing date to complete its initial review of a standard NDA for a new molecular entity, or NME, and make a decision on the application. For priority review applications, the FDA has set the review goal of reviewing NME NDAs within six months of the 60-day filing date. Such deadlines are referred to as the PDUFA date. The PDUFA date is only a goal, and the FDA does not always meet its PDUFA dates. The review process and the PDUFA date may also be extended if the FDA requests or the NDA sponsor otherwise provides additional information or clarification regarding the submission during the review period that amends the original application.

Once the FDA's review of the application is complete, the FDA will issue either a Complete Response Letter, or CRL, or approval letter. A CRL indicates that the review cycle of the application is complete, and the application is not ready for approval. A CRL generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA and may require additional clinical or preclinical testing or other information or analyses in order for the FDA to reconsider the application in the future. Even with the submission of additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA may issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

The FDA may delay or refuse approval of an NDA if applicable regulatory criteria are not satisfied, require additional testing or information, require post-marketing testing and surveillance to monitor safety or efficacy of a product and/or impose other conditions, including distribution restrictions or other risk management mechanisms. For example, the FDA may require a Risk Evaluation and Mitigation Strategy, or REMS, as a condition of approval or following approval to mitigate any identified or suspected serious risks and ensure safe use of the drug. The FDA may prevent or limit further marketing of a product or impose additional post-marketing requirements, based on the results of post-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes, and additional labeling claims, are subject to further testing requirements, FDA notification, and FDA review and approval. Further, should new safety information arise, additional testing, product labeling or FDA notification may be required.

If regulatory approval of a product is granted, such approval may entail limitations on the indicated uses for which such product may be marketed or may include contraindications, warnings or precautions in the product labeling, which has resulted in a boxed warning. A boxed warning is the strictest warning put in the labeling of prescription drugs or drug products by the FDA when there is reasonable evidence of an association of a serious hazard with the drug. The FDA also may not approve the inclusion of all labeling claims sought by an applicant. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing regulatory standards is not maintained or if problems occur after the product reaches the marketplace. In addition, the FDA may require Phase 4 post-marketing studies to monitor the effect of approved products and may limit further marketing of the product based on the results of these post-marketing studies.

#### ***U.S. Post-Approval Requirements***

Any products manufactured or distributed by us pursuant to FDA approvals are subject to continuing regulation by the FDA, including periodic reporting, product sampling and distribution, advertising, promotion, drug shortage reporting, compliance with any post-approval requirements imposed as a conditional of approval such as Phase 4 clinical trials, REMS and surveillance, recordkeeping and reporting requirements, including adverse experiences.

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 fee requirements for approved products, as well as new application fees for supplemental applications with clinical data. Drug manufacturers and their subcontractors, and those supplying products, ingredients, and components of them, are required to register their establishments with the FDA and certain state agencies, and to list their drug products, and are subject to periodic announced and unannounced inspections by the FDA, and these state agencies for compliance with cGMPs and other requirements, which impose procedural and documentation requirements.

Changes to the manufacturing process are strictly regulated and often require prior FDA approval or notification before being implemented. FDA regulations also require investigation and correction of any deviations from cGMPs and specifications, and impose reporting and documentation requirements upon the sponsor, and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

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 withdrawal of marketing approval, mandatory revisions to the approved labeling to add new safety information or other limitations, imposition of post-market studies or clinical trials to assess new safety risks or imposition of distribution or other restrictions under a REMS program, among other consequences.

The FDA closely regulates the marketing and promotion of drugs. A company can make only those claims relating to safety and efficacy that are consistent with the FDA approved labeling. Physicians, in their independent professional medical judgement, may prescribe 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. However, manufacturers and third parties acting on their behalf are prohibited from marketing or promoting drugs in a manner inconsistent with the approved labeling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

Failure to comply with any of the FDA's requirements could result in significant adverse enforcement actions. These include a variety of administrative or judicial sanctions, such as refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, imposition of a clinical hold or termination of clinical trials, warning letters, untitled letters, modification of promotional materials or labeling, product recalls, product seizures or detentions, refusal to allow imports or exports, total or partial suspension of production or distribution, debarment, injunctions, fines, consent decrees, corporate integrity agreements, refusals of government contracts and new orders under existing contracts, exclusion from participation in federal and state healthcare programs, restitution, disgorgement or civil or criminal penalties, including fines and imprisonment. It is also possible that failure to comply with the FDA's requirements relating to the promotion of prescription drugs may lead to investigations alleging violations of federal and state healthcare fraud and abuse and other laws, as well as state consumer protection laws. Any of these sanctions could result in adverse publicity, among other adverse consequences.

### ***U.S. Marketing Exclusivity***

The FDA provides periods of non-patent regulatory exclusivity, which provides the holder of an approved NDA limited protection from new competition in the marketplace for the innovation represented by its approved drug for a period of three or five years following the FDA's approval of the NDA. Five years of exclusivity are available to new chemical entities, or NCEs. An NCE is a drug that contains no active moiety that has been approved by the FDA in any other NDA. An active moiety is the molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt, including a salt with hydrogen or coordination bonds or other noncovalent bonds not involving the sharing of electron pairs between atoms, derivatives, such as a complex (i.e., formed by the chemical interaction of two compounds), chelate (i.e., a chemical compound) or clathrate (i.e., a polymer framework that traps molecules) of the molecule, responsible for the therapeutic activity of the drug substance. During the exclusivity period, the FDA may not accept for review or approve an Abbreviated New Drug Application, or ANDA, or a 505(b)(2) NDA submitted by another company that contains the previously approved active moiety. An ANDA or 505(b)(2) application, however, may be submitted one year before NCE exclusivity expires if a Paragraph IV certification is filed.

### ***Regulation Outside the United States***

We will be subject to similar foreign laws and regulations concerning the development of our product candidates outside of the United States, including the European Union, or EU, and China.

### ***European Union Drug Development***

In the EU, our product candidates also will be subject to extensive regulatory requirements. As in the United States, medicinal products can be marketed only if a marketing authorization from the competent regulatory agencies has been obtained, and the various phases of preclinical and clinical research in the EU are subject to significant regulatory controls.

In April 2014, the EU adopted the Clinical Trials Regulation EU No 536/2014, which replaced the Clinical Trials Directive 2001/20/EC on January 31, 2022. The main characteristics of the new Clinical Trials Regulation include: a streamlined application procedure via a single-entry point through the Clinical Trials Information System, or CTIS; a single set of documents to be prepared and submitted for the application, as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts (Part I contains scientific and medicinal product documentation and Part II contains the national and patient-level documentation). Part I is assessed by a coordinated review by the competent authorities of all EU Member States in which an application for authorization of a clinical trial has been submitted (Member States concerned) of a draft report prepared by a Reference Member State. Part II is assessed separately by each Member State concerned. Strict deadlines have been established for the assessment of clinical trial applications. The role of the relevant ethics committees in the assessment procedure will continue to be governed by the national law of the concerned EU Member State. However, overall related

timelines will be defined by the Clinical Trials Regulation. The Clinical Trial Regulation will have a transition period of three years from the date it became effective.

In the EU, the Pediatric Committee, or PDCO of the EMA must approve the pediatric investigation plan, or PIP, prior to filing a Marketing Authorization Application, or MAA, unless the EMA has granted (1) a product-specific waiver, (2) a class waiver or (3) a deferral for one or more of the measures included in the PIP. The PIP outlines the pharmaceutical company's strategy for investigation of the new medicinal product in the pediatric population. Before an MAA can be filed, or an existing marketing authorization can be amended, the EMA determines that companies actually comply with the agreed studies and measures listed in each relevant PIP. If an applicant obtains a marketing authorization in all EU Member States, or a marketing authorization granted in the centralized procedure by the EC, and the study results for the pediatric population are included in the product information, even when negative, the medicine is then eligible for an additional six-month period of qualifying patent protection through extension of the term of any supplementary protection certificate, or SPC, so long as an application for this extension is made at the same time as filing the SPC application for the product, or at any point up to two years before the SPC expires. In the case of orphan medicinal products, a two-year extension of the orphan market exclusivity may be available. This pediatric reward is subject to specific conditions and is not automatically available when data in compliance with the PIP are developed and submitted.

#### ***European Union Expedited Review and Development***

PRIME, or PRiority MEDicine, is a scheme provided by the EMA to enhance support for the development of medicines that target an unmet medical need and provides accelerated assessment of products representing substantial innovation where the MAA will be made through the centralized procedure. To qualify for PRIME, product candidates require early clinical evidence that the therapy has the potential to offer a major therapeutic advantage over existing treatments or benefits patients without treatment options. Products from small-and medium-sized enterprises, or SMEs, may qualify for earlier entry into the PRIME scheme than larger companies. Among the benefits of PRIME are the appointment of a rapporteur to provide continuous support and help build knowledge ahead of an MAA, early dialogue and scientific advice at key development milestones, and the potential to qualify products for accelerated review earlier in the application process. The receipt of PRIME designation does not change the standards for approval but may expedite the development or approval process. Where, during the course of development, a product no longer meets the eligibility criteria, support under the PRIME scheme may be withdrawn.

#### ***European Union Drug Review and Approval***

In the EU, medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA. There are two types of MAs. Centralized MAs, which are issued by the EC through the centralized procedure, based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, of the EMA, are valid throughout the EU, and in the additional Member States (Iceland, Liechtenstein and Norway) of the EEA. The centralized procedure is mandatory for certain types of products, such as medicinal products produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy medicinal products (i.e., gene therapy, somatic cell therapy or tissue engineered medicines) and medicinal products containing a new active substance indicated for the treatment of HIV, AIDS, cancer, neurodegenerative disorders, diabetes, autoimmune and other immune dysfunctions and viral diseases. The centralized procedure is optional for products containing a new active substance not yet authorized in the EU, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU.

National MAs, which are issued by the competent authorities of the EU Member States and only cover their respective territory, are available for products not falling within the mandatory scope of the centralized procedure. Where a product has already been authorized for marketing in an EU Member State, this national MA can be recognized in another Member State through the mutual recognition procedure. If the product has not received a national MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the decentralized procedure. Under the decentralized procedure an identical dossier is submitted to the competent authorities of each of the Member States in which the MA is sought, one of which is selected by the applicant as the reference Member State, or RMS. The competent authority of the RMS prepares a draft assessment report, a draft summary of the product characteristics, or SmPC, and a draft of the labeling and package leaflet, which are sent to the other Member States (referred to as the Member States Concerned) for their approval. If the Member States Concerned raise no objections, based on a potential serious risk to public health, to the assessment, SmPC, labeling, or packaging proposed by the RMS, the product is subsequently granted a national MA in all the Member States (i.e., in the RMS and the Member States Concerned).

Under the above described procedures, before granting the MA, the EMA or the competent authorities of the EU Member States make an assessment of the risk benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

A pediatric-use marketing authorization, or PUMA, is available for medicines that are already authorized, no longer covered by an SPC or patent that qualifies as an SPC and to be exclusively development for use in children. A PUMA is a

dedicated MA covering the indication and formulation of a medicinal product developed exclusively for use in the pediatric population, where such development has been in accordance with an approved PIP. There are various incentives to apply for a PUMA, including access to the centralized procedure even where the product would otherwise fall outside the mandatory scope of this procedure.

### ***Drug Development in China***

All clinical trials conducted in China for the purpose of seeking marketing approvals must be approved by the China National Medical Products Administration, or NMPA, and conducted at hospitals satisfying GCP requirements. In addition to a standalone China trial to support development, imported drug applicants may include Chinese clinical sites as part of an international multi-center trial, or IMCT. Domestically manufactured drugs are not subject to foreign approval requirements, and in contrast to prior practice, the NMPA has decided to permit those drugs to conduct development via an IMCT as well.

The Drug Administration Law of the PRC, which was revised in 2019, or the rDAL, has now adopted an implied approval system for clinical trials of new drugs. Trials can proceed if, after 60 business days, the applicant has not received any objections from the Center for Drug Evaluation, or CDE, as opposed to the lengthier previous clinical trial pre-approval process in which the applicant had to wait for affirmative approval. The rDAL also expands the number of trial sites by abolishing the GCP accreditation system and requiring trial sites to follow a more simplified notification procedure.

The NMPA finalized in November 2021 the Guideline on Clinical Value-Oriented Research and Development for Oncology Drugs as part of its policies intended to encourage the research and development of innovative oncology drugs with significant clinical value, and discourage repeated research and development of “me-too” drugs with minimal or no clinical value to patients.

Clinical trials conducted in China must be registered and published through the Drug Clinical Trial Information Platform (<http://www.chinadrugtrials.org.cn>). Applicants are required to pre-register the trial information within one month after obtaining the clinical trial approval to obtain the trial’s unique registration number and to complete registration of certain follow-up information before the first subject’s enrollment in the trial. If the foregoing pre-registration and registration is not obtained within one year after obtaining the clinical trial approval, the applicant shall submit an explanation, and if the procedure is not completed within three years, the clinical trial approval automatically expires.

### ***Other Healthcare Laws***

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Our business operations and any current or future arrangements with third-party payors, healthcare providers and physicians may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we develop, market, sell and distribute any drugs for which we obtain marketing approval. In the United States, these laws include, without limitation, state and federal anti-kickback, false claims, physician transparency and patient data privacy and security laws and regulations, including but not limited to those described below.

- The federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing any remuneration (including any kickback, bribe or certain rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward or in return for, either the referral of an individual for, or the purchase order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid. A person or entity need not have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it in order to have committed a violation. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution. Violations are subject to civil and criminal fines and penalties for each violation, plus up to three times the remuneration involved, imprisonment, and exclusion from government healthcare programs;
- The federal civil and criminal false claims laws, including the civil False Claims Act, or FCA, which prohibit individuals or entities from, among other things, knowingly presenting or causing to be presented, to the federal government, claims for payment or approval that are false, fictitious or fraudulent; knowingly making, using or causing to be made or used a false statement or record material to a false or fraudulent claim or obligation to pay or transmit money or property to the federal government; or knowingly concealing or knowingly and improperly avoiding or decreasing an obligation to pay money to the federal government. Manufacturers can be held liable under the FCA even when they do not submit claims directly to government payors if they are deemed to “cause” the submission of false or fraudulent claims. In addition, the government may assert that a claim that includes 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 FCA also permits a private individual acting as a “whistleblower” to bring actions on behalf of the federal government alleging violations of the FCA and to share in any monetary recovery;



- The federal civil monetary penalties laws, which impose civil fines for, among other things, the offering or transfer or remuneration to a Medicare or state healthcare program beneficiary if the person knows or should know it is likely to influence the beneficiary's selection of a particular provider, practitioner or supplier of services reimbursable by Medicare or a state health care program, unless an exception applies. The government may also assert that a claim including items or services resulting from a violation of the federal Anti-Kickback statute constitutes a false or fraudulent claim under federal civil monetary penalties laws;
- The Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for knowingly and willfully executing a scheme or attempting to execute a scheme, to defraud any healthcare benefit program, including private payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense or falsifying, concealing or covering up a material fact or making any materially false statements in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity need not have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their respective implementing regulations, imposes, among other things, specified requirements on covered entities and their business associates relating to the privacy and security of individually identifiable health information including mandatory contractual terms and required implementation of technical safeguards of such information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates in some cases, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions;
- The Physician Payments Sunshine Act, enacted as part of the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, the ACA, imposed new annual reporting requirements for certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, for certain payments and "transfers of value" provided to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by such physicians and their immediate family members. Effective January 1, 2022, these reporting obligations extend to include transfers of value made and investment and ownership interested held in the previous year to certain non-physician providers such as physician assistants and nurse practitioners; and
- Analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party-payors, including private insurers, and may be broader in scope than their federal equivalents; state and foreign laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers; state and foreign laws that require drug manufacturers to report information related to drug pricing and payments and other transfers of value to physicians and other healthcare providers and restrict marketing practices or require disclosure of marketing expenditures and pricing information; state and local laws that require the registration of pharmaceutical sales representatives; state and foreign laws that govern the privacy and security of health information in some circumstances. These data privacy and security laws may differ from each other in significant ways and often are not pre-empted by HIPAA, which may complicate compliance efforts.

In addition, pharmaceutical manufacturers may also be subject to federal and state consumer protection and unfair competition laws and regulations, which broadly regulate marketplace activities and that potentially harm consumers.

The distribution of drugs and biological products is subject to additional requirements and regulations, including extensive record-keeping, licensing, storage and security requirements intended to prevent the unauthorized sale of pharmaceutical products.

The full scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform. Federal and state enforcement bodies have continued to increase their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. It is possible that governmental authorities will conclude that our business practices do 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 related governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties,

damages, fines, imprisonment, disgorgement, exclusion from government funded healthcare programs, such as Medicare and Medicaid, reputational harm, additional oversight and reporting obligations if we become subject to a corporate integrity agreement or similar settlement to resolve allegations of non-compliance with these laws and the curtailment or restructuring of our operations. 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 similar actions, penalties and sanctions. Ensuring business arrangements comply with applicable healthcare laws, as well as responding to possible investigations by government authorities, can be time- and resource-consuming and can divert a company's attention from its business.

### ***Coverage and Reimbursement***

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Thus, even if a product candidate is approved, sales of the product will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage and establish adequate reimbursement levels for, the product. In the United States, no uniform policy of coverage and reimbursement for drug products exists among third-party payors. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. The process for determining whether a third-party payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable regulatory approvals. Additionally, companies may also need to provide discounts to purchasers, private health plans or government healthcare programs. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product could reduce physician utilization once the product is approved and have a material adverse effect on sales, our operations and financial condition. Additionally, a third-party payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product and the level of coverage and reimbursement can differ significantly from payor to payor.

The containment of healthcare costs has become a priority of federal, state and foreign governments and the prices of products have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on 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 a company's revenue generated from the sale of any approved products. Coverage policies and third-party payor reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

### ***Healthcare Reform***

In the United States and some foreign jurisdictions, there have been, and likely will continue to be, a number of legislative and regulatory changes and proposed changes regarding the healthcare system directed at broadening the availability of healthcare, improving the quality of healthcare and containing or lowering the cost of healthcare. For example, in March 2010, the United States Congress enacted the ACA, which, among other things, included changes to the coverage and payment for products under government health care programs. The ACA included provisions of importance to our potential product candidate that:

- created an annual, nondeductible fee on any entity that manufactures, or imports specified branded prescription drugs and biologic products, apportioned among these entities according to their market share in certain government healthcare programs;
- expanded eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;

- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price," or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices;
- addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- expanded the types of entities eligible for the 340B drug discount program;
- a licensure framework for follow-on biologic products;
- establishment of a Center for Medicare & Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending;
- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide point-of-sale-discounts off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D; and
- created a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in and conduct comparative clinical effectiveness research, along with funding for such research.

There remain numerous judicial, administrative, executive and legislative 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 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, as well as policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is unclear how other healthcare reform measures of the Biden administrations or other efforts, if any, to challenge repeal or replace the ACA, will impact our business.

Other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, included aggregate reductions of Medicare payments to providers of 2% per fiscal year. These reductions went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2030, with the exception of a temporary suspension from May 1, 2020 through March 31, 2022 due to the COVID-19 pandemic. Following the temporary suspension, a 1% payment reduction began April 1, 2022, and remained through June 30, 2022. The 2% payment reduction resumed on July 1, 2022. In January 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, imaging centers and cancer treatment centers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Further, on December 20, 2019, the 2020 federal spending package permanently eliminated the ACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminated the health insurer tax. It is impossible to determine whether similar taxes could be instated in the future.

Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, CMS may develop new payment and delivery models, such as bundled payment models. In addition, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their commercial products, which has resulted in several Congressional inquiries and proposed and enacted state and federal 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. For example, at the federal level, President Biden signed an Executive Order on July 9, 2021 affirming the administration's policy to (i) support legislative reforms that would lower the prices of prescription drug and biologics, including by allowing Medicare to negotiate drug prices, by imposing inflation caps, and, by supporting the development and market entry of lower-cost generic drugs and biosimilars; and (ii) support the enactment of a public health insurance option. Among other things, the Executive Order also directs HHS to provide a report on actions to combat excessive pricing of prescription drugs, enhance the domestic drug supply chain, reduce the price that the Federal government pays for drugs, and address price gouging in the industry; and directs the FDA to work with states and Indian Tribes that propose to develop section 804 Importation Programs in accordance with the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, and the FDA's implementing regulations. FDA released such implementing regulations on September 24, 2020, which went into effect on November 30, 2020, providing guidance for states to build and submit importation plans for drugs from Canada. On September 25, 2020, CMS stated drugs imported by states under this rule will not be eligible for federal rebates under Section 1927 of the Social Security Act and manufacturers would not report these

drugs for “best price” or Average Manufacturer Price purposes. Since these drugs are not considered covered outpatient drugs, CMS further stated it will not publish a National Average Drug Acquisition Cost for these drugs. If implemented, importation of drugs from Canada may materially and adversely affect the price we receive for any of our product candidates. Further, on November 20, 2020 CMS issued an Interim Final Rule implementing the Most Favored Nation, or MFN, Model under which Medicare Part B reimbursement rates would have been calculated for certain drugs and biologicals based on the lowest price drug manufacturers receive in Organization for Economic Cooperation and Development countries with a similar gross domestic product per capita. However, on December 29, 2021 CMS rescinded the MFN rule. Additionally, on November 30, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. Pursuant to court order, the removal and addition of the aforementioned safe harbors were delayed, and recent legislation imposed a moratorium on implementation of the rule until January 1, 2026. This deadline was pushed back to January 1, 2027 by the Bipartisan Safer Communities Act. The Inflation Reduction Act of 2022, or the IRA, further delayed implementation of this rule to January 1, 2032. Although a number of these and other proposed measures may require authorization through additional legislation to become effective, and the Biden administration may reverse or otherwise change these measures, both the Biden administration and Congress have indicated that they will continue to seek new legislative measures to control drug costs.

In August 2022, the IRA was signed into law. The IRA includes several provisions that could impact our business to varying degrees, including provisions that reduce the out-of-pocket cap for Medicare Part D beneficiaries to \$2,000 starting in 2025, impose new manufacturer financial liability on certain drugs in Medicare Part D, allow the United States government to negotiate Medicare Part B and Part D price caps for certain high-cost drugs and biologics without generic or biosimilar competition, require companies to pay rebates to Medicare for certain drug prices that increase faster than inflation, and delay the rebate rule that would limit the fees that pharmacy benefit managers can charge. Further, under the IRA, orphan drugs are exempted from the Medicare drug price negotiation program, but only if they have one rare disease designation and for which the only approved indication is for that disease or condition. If a product receives multiple rare disease designations or has multiple approved indications, it will not qualify for the orphan drug exemption. The effect of IRA on our business and the healthcare industry in general is not yet known.

Individual states in the United States have also increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures and, in some cases, designed to encourage importation from other countries and bulk purchasing. For example, we may face competition in the United States for our development candidates and investigational medicines, if approved, from therapies sourced from foreign countries that have placed price controls on pharmaceutical products. In the United States, the FDA issued a final guidance document outlining a pathway for manufacturers to obtain an additional National Drug Code for an FDA-approved drug that was originally intended to be marketed in a foreign country and that was authorized for sale in that foreign country. The market implications of the final guidance are unknown at this time. Proponents of drug reimportation may attempt to pass legislation that would directly allow reimportation under certain circumstances. Legislation or regulations allowing the reimportation of drugs, if enacted, could decrease the price we receive for any products that we may develop and adversely affect our future revenues and prospects for profitability. Further, legally mandated price controls on payment amounts by third-party payors or other restrictions could adversely affect our business prospects, financial condition and results of operations. 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 or put pressure on our product pricing.

On May 30, 2018, the Right to Try Act was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.

Outside the United States, ensuring coverage and adequate payment for a product also involves challenges. Pricing of prescription pharmaceuticals is subject to government control in many countries. For example, in Canada, price control legislation for patented medicines is currently undergoing significant change that may have significant effects on profitability for companies selling products in Canada. Pricing negotiations with government authorities can extend well beyond the receipt of regulatory approval for a product and may require a clinical trial that compares the cost-effectiveness

of a product to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in commercialization.

### **Human Capital Resources**

As of December 31, 2022, we had 146 full-time employees, including 66 employees with an M.D. and/or Ph.D. degree. Of these full-time employees, 113 employees were engaged in research and development activities and 33 employees were engaged in general and administrative activities. We presently have nine senior leaders, seven of whom serve as executive officers. None of our employees is represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

We believe that our future success depends upon our continued ability to attract and retain highly skilled employees. We provide our employees with competitive salaries and bonuses, opportunities for equity ownership, development programs that enable continued learning and growth and a robust employment package that promotes well-being across all aspects of their lives, including health care, retirement planning and paid time off. As part of our promotion and retention efforts, we also invest in ongoing development.

We are committed to diversity, equity, and inclusion in the workplace because we believe that a diverse workforce with an inclusive and equitable environment are a critical component to business success. Our goal is to foster a culture in which every employee can flourish, contribute and be their best. With this focus, we have adopted goals that drive diversity, equity and inclusion initiatives across our entire workforce, from working with managers and employees to develop strategies for understanding their own biases and learning inclusive leadership techniques, to promoting the advancement of leaders from different backgrounds and through supporting our local community in their efforts to bridge the opportunity gap for underserved communities. With the establishment of our Diversity, Equity & Inclusion Council in 2022, this will continue to be an ongoing effort where we focus on incorporating our diversity, equity, and inclusion initiatives into how we work each day.

### **Corporate Information**

We were incorporated in October 2015 under the laws of the State of Delaware. Our principal executive offices are located at 490 Arsenal Way, Suite 120, Watertown, Massachusetts 02472, and our telephone number is (617) 231-0700. We have one wholly owned subsidiary, C4T Securities Corporation, a Massachusetts corporation.

### **Available Information**

Our website address is [www.c4therapeutics.com](http://www.c4therapeutics.com). Information on our website is not incorporated by reference herein. We will make available on our website, free of charge, our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, including exhibits, and any amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. The SEC maintains an Internet site, <http://www.sec.gov>, containing reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC.

A copy of our Corporate Governance Guidelines, Code of Business Conduct and Ethics and the charters of the (i) Audit Committee, (ii) Organization, Leadership and Compensation Committee, and (iii) Nominating and Corporate Governance Committee are posted on our website, [www.c4therapeutics.com](http://www.c4therapeutics.com), under the heading “Corporate Governance” and are available in print to any person who requests copies by contacting us by calling (617) 231-0700 or by writing to C4 Therapeutics, Inc., 490 Arsenal Way, Suite 120, Watertown, Massachusetts 02472, Attention: Corporate Secretary.

We intend to use press releases, our company website, including our Investor Relations website, and our LinkedIn, Twitter, and Instagram accounts, which are listed below, as a means of disclosing material non-public information and for complying with our disclosure obligations under Regulation FD.



[www.linkedin.com/company/c4-therapeutics-inc](http://www.linkedin.com/company/c4-therapeutics-inc).



[twitter.com/c4therapeutics](https://twitter.com/c4therapeutics)



[www.instagram.com/c4therapeutics](https://www.instagram.com/c4therapeutics)

## Item 1A. Risk Factors.

*Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below together with all the other information in this Annual Report on Form 10-K, including the section titled “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and our financial statements and related notes appearing at the end of this Annual Report on Form 10-K, in evaluating our company. The risks and uncertainties described below and in our other filings with the SEC, may not be the only ones that we face. The occurrence of any of the events or developments described below, if they actually occur, could harm our business, financial condition, results of operations and growth prospects. As a result, the market price of our common stock could decline, and you may lose all or part of your investment in our common stock.*

### **Risks related to our financial position and need for additional capital**

*We are a clinical-stage biopharmaceutical company and have incurred significant losses since our inception. We expect to incur losses over at least the next several years and may never achieve or maintain profitability.*

We are a clinical-stage biopharmaceutical company with limited operating history. Our net loss was \$128.2 million and \$83.9 million for the years ended December 31, 2022 and 2021, respectively. As of December 31, 2022, we had an accumulated deficit of \$395.9 million. To date, we have not generated any revenue from product sales and have financed our operations primarily through sales of our equity interests, including public offerings of our common stock, proceeds from our collaborations and debt financing. We are still in the early stages of development of our product candidates. As a result, we expect that it will be several years, if ever, before we have a product candidate ready for regulatory approval and commercialization. We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability. To become and remain profitable, we must succeed in developing, obtaining marketing approval for and commercializing products that generate significant revenue. This will require us to be successful in a range of challenging activities, including, without limitation, successfully completing preclinical studies and clinical trials of our product candidates, discovering additional product candidates, establishing arrangements with third parties for the conduct of our clinical trials, procuring clinical- and commercial-scale manufacturing, obtaining marketing approval for our product candidates, manufacturing, marketing and selling any products for which we may obtain marketing approval, identifying collaborators to develop product candidates we identify or additional uses of existing product candidates and successfully completing development of product candidates for our collaboration partners.

We expect to continue to incur significant expenses and increasing operating losses for at least the next several years. We anticipate that our expenses will increase substantially if and as we:

- initiate, conduct, and successfully complete first-in-human and later-stage clinical trials of our product candidates and as we expand the scope of our proprietary research and development portfolios;
- leverage our TORPEDO platform to identify and then advance additional product candidates into preclinical and clinical development;
- expand the capabilities of our TORPEDO platform;
- seek marketing approvals for any product candidates that successfully complete clinical trials;
- ultimately establish a sales, marketing and distribution infrastructure and scale up external manufacturing capabilities to commercialize any products for which we expect to obtain marketing approval;
- advance, expand, maintain and protect our intellectual property portfolio;
- hire additional personnel, including in areas such as clinical development, regulatory, quality, scientific, and general and administrative positions; and
- add operational, financial and management information systems and personnel, including personnel to support our ongoing research and development and potential future commercialization efforts.

Further, we expect to continue to incur additional costs associated with operating as a public company, including significant legal, accounting, insurance, investor relations and other expenses.

Our expenses could increase beyond our expectations if we are required by the FDA, the European Medicines Agency, or other regulatory authorities to perform trials in addition to those that we currently expect, or if we experience any delays in either establishing appropriate manufacturing arrangements for or completing our clinical trials or the clinical development of any of our product candidates.

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 we will incur or when, if ever, 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 would depress the value of our company and could impair our ability to raise capital, maintain our research and development efforts, expand our business or continue operations. A decline in the value of our company, or in the value of our common stock, could also cause you to lose all or part of your investment.

If one or more of the product candidates that we develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing those approved product candidates. Even if we are able to generate revenues from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations.

***We will need substantial additional funding to pursue our business objectives and continue our operations. If we are unable to raise capital when needed, we may be required to delay, limit, reduce or terminate our research or product development programs or future commercialization efforts.***

We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we prepare for and initiate, conduct, and complete our ongoing and planned first-in-human Phase 1/2 clinical trials of our product candidates, advance our TORPEDO platform and continue research and development activities, expand our proprietary research and development portfolios and initiate and continue clinical trials of, and potentially seek marketing approval for, our current and future preclinical programs. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. Further, we expect to continue 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 may be required to delay, limit, reduce or terminate our research, product development programs or any future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

We had cash, cash equivalents, and marketable securities of approximately \$337.1 million as of December 31, 2022. We believe that these funds, together with future payments expected to be received under existing collaboration agreements will be sufficient to fund our existing operating plan through the end of 2024. We have based this estimate on assumptions that may prove to be wrong, and we could deplete our current capital resources sooner than we currently expect. Our future capital requirements will depend on many factors, including:

- the timing, progress, costs and results of our ongoing and planned first-in-human Phase 1/2 clinical trials for our product candidates and any future clinical development of those product candidates;
- the scope, progress, costs and results of our preclinical and clinical development stage programs and our other product candidates and development programs;
- the number and development requirements of other product candidates that we pursue;
- the success of our ongoing collaborations with Roche, Biogen and Calico, the research terms of which, in the cases of Biogen and Calico, will expire this year;
- the costs, timing and outcomes of regulatory review of our product candidates;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive or expect to receive marketing approval;
- the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval and the timing of the receipt of any such revenue;
- any delays or interruptions, including due to the ongoing COVID-19 pandemic, that we experience in our preclinical studies, clinical trials and/or supply chain;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims; and
- our ability to establish collaboration arrangements with other biotechnology or pharmaceutical companies on favorable terms, if at all, for the development or commercialization of our product candidates or access to our TORPEDO platform.

Our current cash, cash equivalents, and marketable securities will not be sufficient for us to fund any of our product candidates through regulatory approval. As a result, we will need to raise substantial additional capital to complete the development and commercialization of our product candidates. Identifying potential product candidates and conducting preclinical studies and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete. We may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of products that we do not expect to be commercially available for several years, if at all. Adequate additional funds may not be available to us on acceptable terms, or at all. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans.

If one or more of the product candidates that we develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing those approved product candidates. Even if we are able to generate revenues from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations.

***We remain early in the development lifecycle, which may make it difficult for you to evaluate the success of our business to date and assess our future viability.***

We commenced operations in late 2015 and our activities to date have been limited to organizing and staffing our company, business planning, raising capital, conducting discovery and research activities, filing patent applications, identifying potential product candidates, developing and advancing our TORPEDO platform, undertaking preclinical studies, establishing arrangements with third parties for the manufacture of initial quantities of our product candidates, and preparing for and conducting early-stage clinical trials. While we have several ongoing clinical trials, all of our other product candidates are still in preclinical development or in the discovery stage. We have not yet demonstrated our ability to successfully complete any clinical trials, obtain marketing approvals, manufacture a commercial-scale product directly or through a third party or conduct sales, marketing and distribution activities necessary for successful product commercialization. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history or if we had already successfully completed some or all of these types of activities in the past.

In addition, as a biopharmaceutical company, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown challenges. We will need to transition at some point from a company with a research and development focus to a company capable of supporting commercial activities and we may not be successful in making that transition.

We expect our financial condition and operating results to continue to fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

***The ongoing global COVID-19 pandemic could continue to adversely impact our business, including our discovery programs, preclinical studies and development programs, supply chain, business development activities, and general corporate matters.***

The ongoing COVID-19 pandemic continues to have impact, both direct and indirect, on businesses and commerce, including ours, as worker shortages have occurred (including within hospitals such as those who conduct our clinical trials), supply chains have been disrupted, facilities and production have been suspended and demand for certain goods and services such as medical services and supplies has spiked. While vaccines are now generally available throughout the world, new COVID-19 variants continue to spread and the impact of existing COVID-19 vaccines remains uncertain. As a result, the future progression of the pandemic, the definition and establishment of a new normal, and its effects on our business and operations continue to remain uncertain and continue to evolve. Government shutdown orders in the U.S. and/or other countries, including localized shutdowns, if put into effect, may impact our discovery programs, preclinical studies and development programs, as well as our supply chain. In addition, any delays in foreign shipments coming into the United States could also impact our preclinical studies, clinical trial plans, or other business operations.

We and our contract manufacturing organizations, or CMOs, and contract research organizations, or CROs, may face disruptions that could affect our ability to initiate, conduct, and complete discovery or preclinical research activities, or clinical trials. These disruptions may arise from staffing shortages or difficulties in procuring items that are essential for our research and development activities, including, due to shortages arising in raw materials used in the manufacturing of our product candidates, laboratory supplies for our preclinical studies and clinical trials or animals that are used for discovery and/or preclinical testing. For example, as recently as February 2022, the FDA acknowledged the worldwide shortage of non-human primates and released guidance encouraging sponsors of clinical trials to consider the use of other



non-rodent species in their non-clinical toxicity studies. However, this guidance is in effect only for the duration of the public health emergency related to COVID-19, as declared by the Department of Health and Human Services and the FDA has announced that it intends to revise and replace this guidance within sixty days following the termination of the public health emergency. As a result, if we were to elect to use an alternate species for our non-clinical toxicity studies under this guidance, it is possible that we might not be able to initiate and conduct the necessary non-clinical toxicity studies in non-human primates in a timely and cost-effective manner in the future if or when this temporary FDA guidance expires. We and our CROs and CMOs may face disruptions related to our clinical trials arising from potential delays in IND-enabling studies, manufacturing disruptions and/or the ability to obtain necessary institutional review board, or IRB, or other necessary site approvals, as well as other delays at clinical trial sites, including delays related to site staffing and resource limitations. To date, we have experienced delays at certain clinical sites that, due to staffing constraints or other internal policy requirements, have not been able to complete site activation activities or enroll patients in our clinical trial as quickly as likely would have been possible absent the ongoing COVID-19 pandemic.

While we were successfully able to raise capital twice during 2020 and once during 2021, the pandemic has caused significant disruptions in the financial markets and may continue to cause these types of disruptions, which could impact our ability to raise additional funds through public offerings and may also contribute to volatility in our stock price and otherwise impact trading in our stock. Moreover, it is possible the pandemic will significantly impact economies worldwide, which could adversely affect our business prospects, financial condition and results of operations. Any significant disruption of global financial markets, reducing our ability to access capital, could negatively affect our liquidity and ability to continue operations.

COVID-19 and actions taken to reduce its spread continue to rapidly evolve. The extent to which COVID-19 may impede the development of our product candidates, reduce the productivity of our employees, disrupt our supply chains, delay our preclinical studies or clinical trials, reduce our access to capital or limit our business development activities, will depend on future developments, which are highly uncertain and cannot be predicted with confidence. To the extent the ongoing COVID-19 pandemic adversely affects our business prospects, financial condition and results of operations, it may also have the effect of heightening many of the other risks described in this “Risk Factors” section, such as those relating to the timing and results of our planned and future clinical trials and our financing needs.

***Our Credit Agreement with Perceptive Credit contains restrictions that limit our flexibility in operating our business.***

In June 2020, we entered into a credit agreement and guaranty, or the Credit Agreement, with Perceptive Credit Holdings III, LP, which arrangement matures in June 2024. The Credit Agreement provided for a \$20.0 million senior secured delayed draw term loan facility, though we only drew down \$12.5 million of that amount and our ability to borrow the remaining \$7.5 million tranche expired in June 2021. The Credit Agreement is secured by a lien on substantially all of our and our subsidiaries’ assets, including, but not limited to, shares of our subsidiaries, our current and future intellectual property, insurance, trade and intercompany receivables, inventory and equipment, and contract rights. The Credit Agreement requires us to meet specified minimum cash requirements, as described below, and contains various affirmative and negative covenants that limit our ability to engage in specified types of transactions. These covenants, which are subject to customary exceptions, limit our ability to, without Perceptive Credit’s prior written consent, effect any of the following, among other things:

- sell, lease, transfer or otherwise dispose of certain assets;
- acquire another company or business or enter into a merger or similar transaction with third parties;
- incur additional indebtedness;
- make investments;
- enter into certain inbound and outbound licenses of intellectual property, subject to certain exceptions;
- encumber or permit liens on certain assets; and
- pay dividends and make other restricted payments with respect to our common stock.

Our board of directors or management team could believe that taking any one of these actions would be in our best interests and the best interests of our stockholders. If that were the case and if we were unable to complete any of these actions because Perceptive Credit does not provide its consent, that could adversely impact our business, financial condition and results of operations.

In addition, we are required to deposit into controlled accounts all cash or other payments received in respect of any and all of our accounts receivable or any other contract or right and interest and, at all times, to maintain a minimum aggregate balance of \$3.0 million in cash in one or more such controlled accounts. These accounts are required to be maintained as cash collateral accounts securing our obligations under the Credit Agreement. Until our obligations under the Credit

Agreement have been discharged, our ability to use the cash amounts held in these controlled accounts in the operation of our business will be limited.

In the event of a default under the Credit Agreement, including, among other things, our failure to make any payment when due or our failure to comply with any provision of the Credit Agreement, subject to customary grace periods, Perceptive Credit could elect to declare all amounts outstanding to be immediately due and payable and terminate all commitments to extend further credit. If we are unable to repay the amounts due under the Credit Agreement, Perceptive Credit could proceed against the collateral granted to it to secure this indebtedness, which could have an adverse effect on our business, financial condition and results of operations.

Perceptive Credit's interests as a lender may not always be aligned with our interests. If our interests come into conflict with those of Perceptive Credit, including in the event of a default under the Credit Agreement, Perceptive Credit may choose to act in its self-interest.

***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 the time, if ever, when we can generate substantial revenue from product sales, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. Although we may receive potential future payments under our collaborations with Biogen, Roche and Calico, we do not currently have any committed external source of funds. If we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted and the terms of any securities we may issue in the future may include liquidation or other preferences that adversely affect your rights as a common stockholder. 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 acquisitions or capital expenditures or declaring dividends. Covenants in the Credit Agreement impose certain limitations and obligations on us, including restrictions on our ability to incur additional debt and to enter into certain business combinations without Perceptive Credit's prior written consent.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us.

#### **Risks related to the discovery and development of our product candidates**

***Our approach to the discovery and development of product candidates based on our TORPEDO platform for targeted protein degradation is unproven, which makes it difficult to predict the time, cost of development and likelihood of successfully developing any products.***

Treating diseases using targeted protein degradation is a new treatment modality. Our future success depends on the successful development of this novel therapeutic approach. Very few small molecule product candidates using targeted protein degradation, such as those developed through our TORPEDO platform, have been tested in humans and none have been approved in the United States or Europe. The data underlying the feasibility of developing these types of therapeutic products is both preliminary and limited. If any adverse learnings are made by other developers of targeted protein degraders, there is a risk that development of our product candidates could be materially impacted. Discovery and development of small molecules that harness the ubiquitin proteasome pathway to degrade protein targets have been impeded largely by the complexities and limited understanding of the functions, biochemistry and structural biology of the specific components of the ubiquitin-proteasome system, including E3 ligases and their required accessory proteins involved in target protein ubiquitination, as well as by challenges of engineering compounds that promote protein-to-protein interactions.

The scientific research that forms the basis of our efforts to develop our degrader product candidates under our TORPEDO platform is ongoing and the scientific evidence to support the feasibility of developing TORPEDO platform-derived therapeutic treatments is both preliminary and limited. Further, certain cancer patients have shown inherent primary resistance to approved drugs that inhibit disease-causing proteins and other patients have developed acquired secondary resistance to these inhibitors. Although we believe our product candidates may have the ability to degrade the specific mutations that confer resistance to currently marketed inhibitors of disease-causing enzymes, any inherent primary or acquired secondary resistance to our product candidates in patients, or if the scientific research that forms the basis of our efforts proves to be contradicted, would prevent or diminish their clinical benefit.

While we have several ongoing clinical trials, at this time, we have not yet completed a clinical trial of any product candidate. As a result, we are only starting to assess the safety of our lead product candidates in patients and we have not yet assessed the safety of any of our other product candidates in humans. Although some of our earlier-stage product

candidates have produced observable results in animal studies, there is a limited safety data set for their effects in animals. In addition, these product candidates may not demonstrate the same chemical and pharmacological properties in humans and may interact with human biological systems in unforeseen, ineffective or harmful ways. As a result, there could be adverse effects from treatment with any of our current or future product candidates that we cannot predict at this time.

Additionally, the regulatory approval process for novel product candidates such as ours can be more expensive and take longer than for other, better-known or extensively studied product candidates. Although other companies are also developing therapeutics based on targeted protein degradation, no regulatory authority has granted approval for any therapeutic of this nature at this time. As a result, it is more difficult for us to predict the time and cost of developing our product candidates and we cannot predict whether the application of our TORPEDO platform, or any similar or competitive protein degradation platforms, will result in the development of product candidates that make it through to marketing approval. Any development problems we experience in the future related to our TORPEDO platform or any of our research programs may cause significant delays or unanticipated costs or may prevent the development of a commercially viable product. Any of these factors may prevent us from completing our preclinical studies or any clinical trials that we may initiate, as well as from commercializing any product candidates we may develop on a timely or profitable basis, if at all.

***We are a clinical stage biotechnology company and, while we have commenced clinical trials of certain of our product candidates and expect to file an IND for CFT8919, all of our other product candidates are still in preclinical development or in the discovery stage. If we are unable to advance to clinical development, develop, obtain regulatory approval for and commercialize our product candidates or experience significant delays in doing so, our business may be materially harmed.***

We are a clinical-stage biotechnology company and, while we commenced clinical trials of some of our product candidates and expect to file an IND for CFT8919 in the first half of 2023, all of our other product candidates are currently in preclinical development or in the discovery stage. As a result, their risk of failure is high. We have invested substantially all of our efforts and financial resources into building our TORPEDO platform and identifying and conducting preclinical development of our current product candidates, including our lead programs. Our ability to generate revenue from product sales, which we do not expect will occur for several years, if ever, will depend heavily on the successful development and eventual commercialization of one or more of our product candidates. The success of our product candidates will depend on several factors, including the following:

- sufficiency of our financial and other resources;
- successful initiations and completion of preclinical studies;
- successful submission and clearance of INDs and initiation of clinical trials;
- successful patient enrollment in, and conduct and completion of, clinical trials;
- receipt and related terms of marketing approvals from applicable regulatory authorities;
- obtaining and maintaining patent or trade secret protection and regulatory exclusivity for our product candidates;
- making suitable arrangements with third-party manufacturers for both clinical and commercial supplies of our product candidates;
- developing product candidates that achieve the therapeutic properties desired and appropriate for their intended indications;
- establishing sales, marketing and distribution capabilities and launching commercial sales of our products, if and when approved, whether alone or in collaboration with others;
- acceptance of our products, if and when approved, by patients, the medical community and third-party payors;
- obtaining and maintaining third-party coverage and adequate reimbursement;
- establishing a continued acceptable safety profile of our products and maintaining that profile following approval; and
- effectively competing with other therapies.

If we do not successfully achieve one or more of these factors in a timely manner, or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, which could materially harm our business. Moreover, if we do not receive regulatory approvals, we may not be able to continue our operations.

***We have relatively limited experience as a company in completing preclinical studies to enable the filing of INDs, submitting INDs or commencing, enrolling and conducting clinical trials.***

Our experience as a company in completing IND-enabling preclinical studies comes from our work in commencing clinical development of three product candidates. In addition, we are planning to submit an IND application for a Phase 1 clinical trial of CFT8919 in EGFR L858R NSCLC in 2023. While this work represents a substantial amount of progress, to date, we still have relatively limited experience as a company in commencing, enrolling and conducting clinical trials. In part because of this, while we continue to make strides in this area, we cannot be certain that our preclinical studies will be completed on time, that we will submit INDs in a timely manner, that any INDs we submit will be cleared by the FDA in a timely manner, if at all, or if our planned clinical trials will begin, enroll or be completed on time, if at all. In addition, while these are our current expectations, we may experience manufacturing delays or other delays with IND-enabling studies, we may determine that additional IND-enabling studies are warranted or we may face delays due to the ongoing COVID-19 pandemic. Moreover, we cannot be sure that submission of an IND will result in the FDA allowing us to commence clinical trials or that, once begun, issues will not arise that lead to the suspension or termination of our clinical trials. Additionally, even if the applicable regulatory authorities agree with the design and implementation of the clinical trials set forth in our INDs, we cannot guarantee that those regulatory authorities will not change their requirements in the future. These considerations apply to the INDs described above and also to new clinical trials we may submit as amendments to existing INDs or as part of new INDs in the future. Any failure to file INDs on the timelines we expect or to obtain regulatory approvals for our clinical trials may prevent us from completing our clinical trials or commercializing our products on a timely basis, if at all.

Further, large-scale clinical trials would require significant additional financial and management resources and reliance on third-party clinical investigators and consultants. Relying on third-party clinical investigators, CROs and consultants may cause us to encounter delays that are outside of our control and, for each of the product candidates that is currently in clinical development, we have engaged a CRO to lead our first-in-human Phase 1/2 clinical trial. Relying on third parties in the conduct of our preclinical studies or clinical trials exposes us to a risk that they may not adequately adhere to study or trial protocols or comply with good laboratory practice or good clinical practice, or GCP, as required for any studies or trials we plan to submit to a regulatory authority. We may also be unable to identify and contract with sufficient investigators, CROs and consultants on a timely basis or at all, and we may also determine and have in the past determined after a clinical trial has commenced that a change in CRO is warranted. There can be no assurance that we will be able to negotiate and enter into appropriate contractual arrangements without current or potential future CROs, if and when necessary for our other product candidates, on terms that are acceptable to us on a timely basis or at all.

***Our preclinical studies and clinical trials may fail to demonstrate adequately the safety and efficacy of any of our product candidates, which would prevent or delay development, regulatory approval, and commercialization. Further, the results of preclinical studies may not be predictive of future results in later studies or trials and initial success in clinical trials may not be indicative of results obtained when these trials are completed or in later stage clinical trials.***

Before obtaining regulatory approval for the commercial sale of any of our product candidates, we must demonstrate through lengthy, complex and expensive preclinical studies and clinical trials that our product candidates are both safe and effective for use in each target indication. Preclinical and clinical testing is expensive and can take many years to complete. Further, the outcome of these activities is inherently uncertain. Failure can occur at any time during the preclinical study and clinical trial processes and, because many of our product candidates are in an early stage of development and have never been tested in humans, there is a high risk of failure. In addition, because targeted protein degraders are a relatively new class of product candidates, any failures or adverse outcomes in preclinical or clinical testing seen by other developers in this class could materially impact the success of our programs. We may never succeed in developing marketable products.

It is also possible that the results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. Preclinical and clinical data are often susceptible to varying interpretations and analyses and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. Although product candidates may demonstrate promising results in preclinical studies and early clinical trials, they may not prove to be effective or safe in subsequent clinical trials. The results of the dose escalation portion of our ongoing and planned first-in-human Phase 1/2 clinical trials of our product candidates may not be predictive of the results of further clinical trials of these product candidates or any of our other product candidates and may not be sufficient to enable us to progress to the Phase 2 portion of a Phase 1/2 clinical trial. Testing on animals occurs under different conditions than testing in humans and, therefore, the results of animal studies may not accurately predict human experience.

There is typically an extremely high rate of attrition from the failure of product candidates proceeding through preclinical studies and clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and

efficacy profile despite having progressed successfully through preclinical studies and/or initial clinical trials. Likewise, early, smaller-scale clinical trials may not be predictive of eventual safety or effectiveness in large-scale pivotal clinical trials. Many companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy, insufficient durability of efficacy or unacceptable safety issues, notwithstanding promising results in earlier trials. Most product candidates that commence preclinical studies and clinical trials are never approved as products. Any setbacks of this nature in our clinical development could materially harm our business, financial condition, results of operations and prospects. Further, initial success in our clinical trials may not be indicative of results obtained when those trials are completed or in any later stage clinical trials we may conduct. In particular, the small number of patients in our planned early clinical trials or the designs of these trials may make the results of these trials less predictive of the outcome of later clinical trials.

Additionally, we expect that the first clinical trials for our product candidates will be open-label studies, where both the patient and investigator know whether the patient is receiving the investigational product candidate or either an existing approved drug or placebo. This is the case with our ongoing first-in-human clinical trials and will be the case in the first-in-human clinical trials of the additional product candidates we presently expect to advance into clinical development. Most typically, open-label clinical trials test only the investigational product candidate and sometimes do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open-label clinical trials are aware when they are receiving treatment. In addition, open-label clinical trials may be subject to an “investigator bias” where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge.

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

While we have commenced a clinical trial of each of our three most advanced product candidates and have plans to do the same for our fourth product candidate, CFT8919, we have not yet initiated clinical trials for any of our other product candidates. As is the case with all drugs, it is likely that there may be side effects associated with the use of our product candidates related to on-target toxicity, off-target toxicity, or other mechanisms of drug toxicity including chemical-based toxicity. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects of this nature. If unacceptable levels of toxicity are observed or if our product candidates have other characteristics that are unexpected, we may need to abandon their development, modify our development plans as to dose level and/or dose schedule or otherwise, or limit development to more narrow uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. For example, due to observed safety signals, we previously modified the dosing schedule in our ongoing Phase 1/2 clinical trial of CFT7455 as we continue to advance this clinical trial. Further, if we were to observe unacceptable levels of side effects, or if other developers of similar targeted protein degraders were to find an unacceptable severity or prevalence of side effects with their drug candidates, our trials could be suspended or terminated, and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. Drug-related side effects could also affect patient recruitment or the ability of enrolled patients to complete an ongoing trial or result in potential product liability claims. 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. Any of these occurrences may significantly harm our business, financial condition, and prospects.

***The conclusions and analysis drawn from announced or published interim top-line and preliminary data from our clinical trials from time to time may change as more patient data become available. Further, all interim data that we provide remains subject to audit and verification procedures that could result in material changes in the final data.***

From time to time, we may publish interim top-line or preliminary data from our clinical trials. Interim data from clinical trials that we may conduct 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. In addition, preliminary or top-line data also remain subject to audit and verification procedures that may result in the final data being different, potentially in material ways, from the preliminary data we previously announced or published. As a result, interim and preliminary data should be viewed with

caution until final data are available. Adverse differences between preliminary or interim data and final data could significantly harm our reputation, business, financial condition, results of operations and prospects.

***Drug development is a lengthy and expensive process with an uncertain outcome. We may incur unexpected costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.***

While we have commenced clinical trials of our three most advanced product candidates and expect to file an IND for our fourth product candidate, CFT8919, in the first half of 2023, all of our other product candidates are still in preclinical development or in the discovery stage at this time and the risk of failure for all of our product candidates remains high. We are unable to predict when or if any of our product candidates will prove effective or safe in humans or will receive marketing approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Before we can commence clinical trials for a product candidate, we must complete extensive preclinical studies that support our planned INDs in the United States or similar applications in other jurisdictions. We cannot be certain of the timely initiation, completion or outcome of our preclinical studies and, other than in the cases of our three most advanced product candidates where the FDA has cleared the IND for our first-in-human studies of the drug candidate, we cannot predict if the FDA or similar regulatory authorities outside the United States will allow us to commence our proposed clinical trials or if the outcome of our preclinical studies ultimately will support the further development of any of our product candidates.

Clinical testing is expensive, difficult to design and implement, can take many years to enroll and complete and is uncertain as to the timing and outcome. A failure of one or more clinical trials can occur at any stage of the process. We may experience numerous unforeseen events during or as a result of clinical trials, which could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- delays in reaching, or the failure to reach, a consensus with regulators on clinical trial design or the inability to produce acceptable preclinical results to enable entry into human clinical trials;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials may be insufficient or inadequate, including as a result of delays in the testing, validation, manufacturing and delivery of product candidates to the clinical sites by us or by third parties with whom we have contracted to perform certain of those functions;
- delays in reaching, or the failure to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites or CROs;
- the failure of regulators or IRBs to authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- difficulty in designing clinical trials and in selecting endpoints for diseases that have not been well studied and for which the natural history and course of the disease is poorly understood;
- the selection of certain clinical endpoints that may require prolonged periods of clinical observation or analysis of the resulting data;
- the number of patients required for clinical trials of our product candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate, participants may drop out of these clinical trials at a higher rate than we anticipate or fail to return for post-treatment follow-up or we may be unable to recruit suitable patients to participate in our clinical trials;
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or IRBs to suspend or terminate our clinical trials;
- we may have to suspend or terminate clinical trials of our product candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks;
- the third parties with whom we contract may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- the requirement from regulators or IRBs that we or our investigators suspend or terminate clinical trials for various reasons, including noncompliance with regulatory requirements or unacceptable safety risks;
- clinical trials of our product candidates may produce negative or inconclusive results and we may decide, or regulators may require us, to conduct additional clinical trials, modify our development plans as to dose level and/pr dose schedule or otherwise, or abandon product development programs;

- the cost of clinical trials of our product candidates may be greater than we anticipate;
- staffing shortages, including but not limited to the lack of appropriately trained or experienced clinical research associates or medical staff at the institutions where we conduct our clinical trials or the lack of sufficient support personnel at these institutions involved in site contracting and activation, may cause delays or create other challenges to the timely and efficient conduct of our clinical trials;
- imposition of a clinical hold by regulatory authorities as a result of a serious adverse event, concerns with a class of product candidates or after an inspection of our clinical trial operations, trial sites or manufacturing facilities;
- occurrence of serious adverse events associated with the product candidate that are viewed to outweigh its potential benefits; and
- disruptions caused by the continuing spread and effects of the ongoing COVID-19 pandemic may increase the likelihood that we encounter these types of difficulties or cause other delays in initiating, enrolling, conducting or completing our planned clinical trials.

We also may encounter challenges due to evolving regulatory policy. For example, the FDA's Oncology Center of Excellence launched Project Optimus, an initiative by to reform dose selection in oncology drug development, in 2021 and is still being implemented. If the FDA believes we have not sufficiently established that the selected dose or doses for our product candidates maximize efficacy as well as safety and tolerability, the FDA may require us to conduct additional clinical trials or generate additional dosing-related information, which could significantly delay and/or increase the expense of our clinical development programs.

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

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

Our product development costs also will increase if we experience delays in preclinical studies or clinical trials or in obtaining marketing approvals. While we have commenced clinical trials of our three most advanced product candidates and expect to file an IND for our fourth product candidate, CFT8919, in the first half of 2023, we do not know whether any of our other preclinical studies or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant preclinical study or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or could allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates, which may harm our business, results of operations, financial condition and prospects.

Further, cancer therapies sometimes are characterized as first-line, second-line or third-line. The FDA often approves new oncology therapies initially only for third-line or later use, meaning for use after two or more other treatments have failed. When cancer is detected early enough, first-line therapy, usually systemic anti-cancer therapy (e.g., chemotherapy), surgery, radiation therapy or a combination of these, is sometimes adequate to cure the cancer or prolong life without a cure. Second-line and third-line therapies are administered to patients when prior therapy has been shown to not be effective. Our ongoing and planned early-stage clinical trials will be with patients who have received one or more prior treatments and we expect that we would initially seek regulatory approval of our lead product candidates as second-line or third-line therapy. Subsequently, for those products that prove to be sufficiently beneficial, if any, we would expect to seek approval potentially as a first-line therapy, but any product candidates we develop, even if approved for second-line or third-line therapy, may not be approved for first-line therapy and, prior to seeking and/or receiving any approvals for first-line therapy, we may have to conduct additional clinical trials.

***Targeted protein degradation is a novel modality that continues to attract substantial interest from existing and emerging biotechnology and pharmaceutical companies. As a result, we face substantial competition, which may result in others discovering, developing or commercializing products for the same indication and/or patient population before or more successfully than we do.***

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. We face, and will continue to face, competition from third parties that use protein degradation, antibody therapy, inhibitory nucleic acid, immunotherapy, gene editing or gene therapy development platforms and from companies focused on more traditional therapeutic modalities, such as small molecule inhibitors. The competition we face and will face is likely to come from multiple sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions, government agencies and public and private research institutions.

Targeted protein degradation is an emerging therapeutic modality that has the potential to deliver therapies that improve outcomes for patients. As a result, a number of biotechnology and pharmaceutical companies are already working to develop degradation-based therapies and the number of companies entering this space continues to increase. We are aware of several biotechnology companies developing product candidates based on chimeric small molecules for targeted protein degradation including Arvinas, Inc., Astellas Pharma Inc., BioTheryX, Inc., Captor Therapeutics, Inc., Cullgen Inc., Foghorn Therapeutics, Inc., Frontier Medicines Corporation, Haisco Pharmaceutical Group, Kymera Therapeutics, Inc., Monte Rosa Therapeutics, Inc., Nurix Therapeutics, Inc., PhoreMost, Ltd., Plexium, Inc., Proteovant Therapeutics, Inc., Salaris Pharmaceuticals, Inc., Seed Therapeutics, Inc., and Vividion Therapeutics, Inc. (a subsidiary of Bayer AG). Further, several large pharmaceutical companies and academic institutions have disclosed investments and research in this field including Amgen, AstraZeneca plc, Bristol-Myers Squibb Company (and its subsidiary Celgene Corporation), GlaxoSmithKline plc, Genentech, Inc. and Novartis International AG. In addition to competition from other protein degradation therapies, any products that we develop may also face competition from other types of therapies, such as small molecule, antibody, T cell or gene therapies. For example, we understand that Adaptimmune Limited, Foghorn Therapeutics, Inc. and GlaxoSmithKline plc are pursuing the development of therapies for patients with synovial sarcoma.

Many of our current or potential competitors, either alone or with their collaboration partners, have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our product candidates. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors, the scale of which could be difficult to compete against. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any product candidate that we may develop. Our competitors also may obtain FDA or other regulatory approval for their product candidates more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic products. There are generic products currently on the market for certain of the indications that we are pursuing, and additional products are expected to become available on a generic basis over the coming years. If our product candidates are approved, we expect that they will be priced at a significant premium over competitive generic products.

***Our ability to use our net operating loss carryforwards and research and development tax credit carryforwards may be limited.***

As of December 31, 2022, we had \$171.6 million federal net operating loss carryforwards and \$273.6 million gross in U.S. state net operating loss carryforwards, portions of which expire at various dates through 2041. Under current law, federal net operating losses generated in tax years beginning after 2017, if any, will not expire and may be carried forward indefinitely, but our ability to deduct such federal net operating losses in tax years beginning after December 31, 2020 will be limited to the lesser of the net operating loss carryover or 80% of the corporation's adjusted taxable income (subject to Section 382 of the Internal Revenue Code of 1986, as amended). The Coronavirus Aid, Relief, Economic Security Act, or CARES Act, temporarily allows us to carryback net operating losses arising in 2018, 2019 and 2020 to the five prior years. It is uncertain how various states will respond to the CARES Act or any newly enacted federal tax law. In addition, at the state level, there may be periods during which the use of net operating losses is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.



As of December 31, 2022, we also had U.S. federal and state research and development tax credit carryforwards of \$9.1 million and \$2.9 million, respectively, which expire at various dates through 2041. These tax credit carryforwards could expire unused and be unavailable to offset our future income tax liabilities.

In addition, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, and corresponding provisions of state law, if a corporation undergoes an “ownership change,” which is generally defined as a greater than 50% change, by value, in its equity ownership over a three-year period, the corporation’s ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change income or taxes may be limited. In 2021, we completed a study of ownership changes from inception through December 31, 2020, which concluded that we experienced ownership changes as defined by Section 382 of the Code. However, there were no net operating loss carryforwards that were limited or expired unused. We have not updated the study to assess whether a change of ownership has occurred during 2022. We may have experienced additional ownership changes that have not been identified that could result in the expiration of our net operating loss and tax credit carryforwards before utilization and we may experience subsequent shifts in our stock ownership, some of which are outside our control. As a result, if we earn net taxable income and determine that an ownership change has occurred and our ability to use our historical net operating loss and tax credit carryforwards is materially limited, that will harm our future operating results by effectively increasing our future tax obligations.

***If serious adverse events, undesirable side effects or unexpected characteristics are identified during the development of any product candidates we may develop, we may need to modify, abandon or limit our further clinical development of those product candidates.***

While we have commenced clinical trials of our three most advanced product candidates and expect to expect to file an IND for our fourth product candidate, CFT8919, in the first half of 2023, all of our other product candidates are still in the preclinical or discovery stages at this time, which means that we have not yet evaluated any of our other product candidates in human clinical trials. It is impossible to predict when or if any product candidates we may develop will prove safe in humans. There can be no assurance that any of the product candidates developed through our TORPEDO platform will not cause undesirable side effects, which could arise at any time during preclinical or clinical development.

A potential risk with product candidates developed through our TORPEDO platform, or in any protein degradation product candidate, is that healthy proteins or proteins not targeted for degradation will be degraded or that the degradation of the targeted protein in and of itself could cause adverse events, undesirable side effects or unexpected characteristics. There is also the potential risk of delayed adverse events following treatment using product candidates developed through our TORPEDO platform.

If any product candidates we develop are associated with serious adverse events or undesirable side effects or have other characteristics that are unexpected, we may need to abandon their development, modify our development plans as to dose level and/or dose schedule of otherwise, or limit development to certain uses or subpopulations in which the adverse events, undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. The occurrence of any of these types of events would have an adverse effect on our business, financial condition, results of operations and prospects. Many product candidates that initially showed promise in early-stage testing for treating cancer or other diseases have later been found to cause side effects that prevented further clinical development of the product candidates or limited their competitiveness in the market. For example, single agent BRAF inhibitors can cause a secondary malignancy called keratocanthoma, which is a skin cancer caused by paradoxical activation of BRAF upon inhibitor binding.

***If we experience delays or difficulties in the enrollment of patients in our clinical trials, our timelines for submitting for and receiving necessary marketing approvals could be delayed or prevented.***

We may not be able to initiate clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials, as required by the FDA or similar regulatory authorities outside of the United States. We progressed our three most advanced product candidates, CFT7455, CFT8634 and CFT1946, into first-in-human clinical trials in June 2021, May 2021 and December 2022, respectively. In addition, we are planning to file an IND for CFT8919 during the first half of 2023, after which we plan to initiate a first-in-human Phase 1/2 clinical trial for that program. While we believe that we will be able to enroll a sufficient number of patients into each of these clinical trials, we cannot predict with certainty how difficult it will be to enroll patients for trials, some of which are in rare indications, either generally or specifically during the ongoing COVID-19 pandemic. Our ability to identify and enroll eligible patients for clinical trials of our product candidates may turn out to be limited or we may be slower in enrolling these trials than we anticipate. In addition, some of our competitors have ongoing clinical trials for product candidates that treat the same indications as our product candidates and, as a result, patients who would be eligible for our clinical trials

may instead elect to enroll in clinical trials of our competitors' product candidates. Patient enrollment in clinical trials is also affected by other factors including:

- the severity of the disease under investigation;
- the eligibility criteria for the trial in question;
- the perceived risks and benefits of the product candidates offered in the clinical trials;
- the efforts to facilitate timely enrollment in clinical trials;
- the patient referral practices of physicians;
- the availability of suitable and sufficient staffing at clinical trial sites;
- the burden on patients due to the scope and invasiveness of required procedures under clinical trial protocols, some of which may be inconvenient and/or uncomfortable;
- the ability to monitor patients adequately during and after treatment;
- the proximity and availability of clinical trial sites for prospective patients; and
- the impact of the ongoing COVID-19 pandemic, which may affect the conduct of a clinical trial, including by slowing potential enrollment or reducing the number of eligible patients for clinical trials or by interfering with patients' ability to return to the clinical trial site for required monitoring, procedures or follow-up.

Our inability to enroll a sufficient number of patients for our planned clinical trials, or our inability to do so on a timely basis, would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may also result in increased development costs for our product candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing.

***We may expend our limited resources to pursue a particular product candidate or indication 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 research programs and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. 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 collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

***We may develop our product candidates in combination with other drugs. If the FDA or similar regulatory authorities outside of the United States do not approve these other drugs, revoke their approval of these other drugs 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 our product candidates.***

Based on the study design for a number of our product candidates, once a recommended dose is identified from the dose escalation portion of our first-in-human Phase 1/2 clinical trial, we often plan to conduct a portion of that clinical trial in combination with one or more other medicines. We did not develop or obtain marketing approval for, nor do we manufacture or sell, any of the currently approved drugs that we may study in combination with our product candidates. If the FDA or similar regulatory authorities outside of the United States revoke their approval of the drug or drugs we intend to deliver in combination with our product candidates, we will not be able to market our product candidates in combination with those revoked drugs.

If safety or efficacy issues arise with any of these drugs, we could experience significant regulatory delays and the FDA or similar regulatory authorities outside of the United States may require us to redesign or terminate certain of our clinical trials. If the drugs we use are replaced as the standard of care for the indications we choose for our product candidates, the FDA or similar regulatory authorities outside of the United States may require us to conduct additional clinical trials. In addition, if manufacturing or other issues result in a shortage of supply of the drugs with which we determine to combine with our product candidates, we may not be able to complete clinical development of our product candidates on our current timeline or at all.

Even if our product candidates were to receive marketing approval or be commercialized for use in combination with other existing drugs, we would continue to be subject to the risks that the FDA or similar regulatory authorities outside of the

United States could revoke approval of the drugs used in combination with our product candidates or that safety, efficacy, manufacturing or supply issues could arise with these existing drugs.

Combination therapies are commonly used for the treatment of cancer and we would be subject to similar risks if we were to elect to develop any of our other product candidates for use in combination with other drugs or for indications other than cancer. This could result in our own products being removed from the market or being less successful commercially.

***We may not be successful in our efforts to identify or discover additional potential product candidates.***

While our four most advanced programs are focused on oncology targets, a key element of our strategy is to apply our TORPEDO platform to develop product candidates that address a broad array of targets and new therapeutic areas, such as neurodegeneration, diseases of aging and infectious disease. The therapeutic discovery activities that we are conducting may not be successful in identifying product candidates that are useful in treating cancer or other diseases. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for a number of reasons, including:

- potential product candidates may, on further study, be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be drugs that will receive marketing approval or achieve market acceptance;
- potential product candidates may not be effective in treating their targeted diseases; or
- the market size for the target indications of a potential product candidate may diminish over time due to improvements in the standard of care to the point that further development is not warranted.

Research programs to identify new product candidates require substantial technical, financial and human resources. We may choose to focus our efforts and resources on a potential product candidate that ultimately proves to be unsuccessful. If we are unable to identify suitable product candidates for preclinical and clinical development, we will not be able to obtain revenues from sale of products in future periods, which likely would result in significant harm to our financial position and adversely impact our stock price.

***If we do not achieve our projected development goals in the timeframes we announce and expect, the commercialization of our products may be delayed and, as a result, our stock price may decline.***

From time to time, we may estimate the timing of the anticipated accomplishment of various scientific, clinical, regulatory and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of preclinical studies and clinical trials and the submission of regulatory filings. From time to time, we may publicly announce the expected timing of some of these milestones. Each of these milestones is and will be based on numerous assumptions. The actual timing of these milestones can vary dramatically compared to our estimates, in some cases for reasons beyond our control. If we do not meet these milestones as publicly announced, or at all, our revenue may be lower than expected or the commercialization of our products may be delayed or never achieved and, as a result, our stock price may decline.

#### **Risks related to dependence on third parties**

***We expect to rely on third parties to conduct our future clinical trials and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials.***

We currently rely on CROs to conduct our clinical trials, as we currently do not plan to independently conduct clinical trials of any of our product candidates. Additionally, we must contract with third-party research sites for the conduct of our clinical trials. Our agreements with these CROs and sites might terminate for a variety of reasons, including a failure to perform by the third parties. If we were ever to need to enter into alternative arrangements, or if we were to need to change a CRO for an ongoing clinical trial, which we have done in the past, we might experience delays in our clinical development activities.

Our reliance on CROs for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities for how these activities are performed. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols in the applicable IND. Moreover, the FDA requires compliance with standards, commonly referred to as GCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. GCP compliance extends not only to sponsors of clinical research but also to third parties including CROs and sites involved in the conduct of clinical research.

Further, these CROs or sites may have relationships with other entities, some of which may be our peers or competitors. If the CROs or sites with whom we work do not successfully carry out their contractual duties, meet expected deadlines or

conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates.

***Manufacturing pharmaceutical products is complex and subject to product delays or loss for a variety of reasons. We contract with third parties for the manufacture of our product candidates for preclinical testing and clinical trials and expect to continue to do so for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or products or that we will not have the quantities we desire or require at an acceptable cost or quality or at the right time, which could delay, prevent or impair our development or commercialization efforts.***

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We rely on and expect to continue to rely on CMOs for both drug substance and finished drug product. This reliance on third parties may increase the risk that we will not have sufficient quantities of our product candidates or products or that we will not have the quantities we desire or require at an acceptable cost or quality, which could delay, prevent or impair our development or commercialization efforts, including where a pre-approval inspection or an inspection of manufacturing sites is required and due to the ongoing COVID-19 pandemic and travel restrictions, if still then in effect, FDA is unable to complete those required inspections during the review period.

We may be unable to establish agreements with CMOs or to do so on acceptable terms. Even if we are able to establish agreements with CMOs, reliance on third-party manufacturers entails additional risks, including:

- reliance on the third party for regulatory, compliance, quality assurance and manufacturing success;
- the possible breach of the manufacturing agreement by the third-party CMO;
- the possible risk that the CMO will cease offering the services we require or shut down operations altogether, either temporarily or permanently, due to a regulatory concern, financial insolvency, non-compliance with applicable law or another reason;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the possible termination or non-renewal of the agreement by the third party at a time that is costly or inconvenient for us or the inability of the CMO to provide us with a manufacturing slot when we need it.

We have only limited technology transfer agreements in place with respect to our product candidates and these existing arrangements do not extend to commercial supply. We acquire many key materials on a purchase order basis. As a result, we do not have long-term committed arrangements with respect to our product candidates and other materials. If we anticipate receiving or receive marketing approval for any of our product candidates, we will need to establish or have established an agreement for commercial manufacture with one or more third parties.

Third-party manufacturers may not be able to comply with current good manufacturing practices, or cGMP, regulations or similar regulatory requirements outside of the United States. Some of our molecules are highly potent and, in the absence of additional safety data, they receive a high occupational exposure band, or OEB. These assigned OEBs dictate the containment and other precautions that must be taken as part of the manufacture of our product candidates and, for molecules with high OEB designations, serve to limit the number of CMOs who are qualified to manufacture our molecules. Our failure, or the failure of our CMOs, to comply with applicable regulations, including the ability of our CMOs to work with our highly potent materials and the safety protocols in connection therewith, could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, 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 product candidates and any products that we may develop may compete with other product candidates and products for access to manufacturing facilities. As a result, we may not obtain access to these facilities on a priority basis or at all. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us, particularly, in some cases, given the potency or OEB of our compounds.

Any performance failure or delay in performance on the part of our existing or future manufacturers could delay clinical development or marketing authorization. For example, in the past, a CMO with whom we work had a mechanical issue arise in connection with a manufacturing step for a manufacturing run for our CFT7455 product candidate. While this issue did not ultimately delay the timing of submission of our IND for CFT7455, in the future, we could experience a manufacturing issue that would have a material impact on development of our product candidates and the occurrence of an event of this nature would largely be outside of our control. We do not currently have arrangements in place for redundant supply or a second source for drug substance or drug product. If our current CMOs cannot perform as agreed, we may be

required to replace them. Although we believe that there are several potential alternative manufacturers who could manufacture our product candidates, we may incur added costs and delays in identifying and qualifying any replacement manufacturers or we may not be able to reach agreement with any alternative manufacturer. While we have identified alternate vendors for some of the manufacturing work related to certain of our product candidates, switching vendors could result in significant additional costs of materials and significant delays to our operations and we may be constrained in the vendors we can select, particularly for compounds that have high OEB designations.

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.

Additionally, we currently rely on single source suppliers for a portion of our supply chain for our preclinical and clinical trial supplies. If our current or future suppliers, whether for raw materials, drug substance or drug product, are unable to supply us with sufficient materials for our preclinical studies and clinical trials, we may experience delays in our development efforts as we locate and qualify new suppliers or manufacturers.

The third-party manufacturers on whom we rely may incorporate their own proprietary processes into our product candidate manufacturing processes. We have limited control and oversight of a third party's proprietary manufacturing processes. If a third-party manufacturer were to modify its processes, those modifications could negatively impact our manufacturing, including product loss or failure that requires additional manufacturing runs or a change in manufacturer, both of which could significantly increase the cost of and significantly delay the manufacture of our product candidates.

As our product candidates progress through preclinical studies and clinical trials towards approval and commercialization, we expect that various aspects of the product development and manufacturing process will evolve in an effort to optimize processes and results. Some of those product and manufacturing process changes may involve the use of third-party proprietary technology, which could then cause us to need to obtain a license from third parties. In addition, these types of changes may require that we make amendments to our regulatory applications, which could further delay the timeframes under which modified manufacturing processes can be used for any of our product candidates.

In addition, as we advance our product candidates into later stage clinical trials and plan for the potential commercialization of our product candidates, we may determine that it is necessary or appropriate to bring on additional suppliers of drug product and/or drug substance, which could result in changes to the manufacturing processes for our product candidates and may require us to provide additional information to regulatory authorities. If we were to bring on additional CMOs for our product candidates, we may also be required to demonstrate analytical comparability and/or conduct additional bridging studies or trials, all of which would require additional time and expense.

***We have existing collaborations with third parties under which we are engaged in the research, development and commercialization of certain product candidates. If any of these collaborations are not successful, we may not be able to capitalize on the market potential of those product candidates. In addition, these collaborations could impact our intellectual property rights.***

Previously, we entered into the following collaborations, which involve our research programs:

- a collaboration agreement with Roche in December 2015, which we amended and restated in December 2018 and further amended in November 2020 and updated as to included targets in November 2021;
- a collaboration agreement with Calico in March 2017, which was extended in respect of one program in September 2021 and which will expire as to the research term in March 2023; and
- a collaboration agreement with Biogen in December 2018, which was amended in February 2020 and will expire as to the research term in June 2023.

Under these collaboration agreements, we are generally responsible for developing drug candidates leveraging our TORPEDO platform based on partner-selected targets. Further, these agreements provide that our collaboration partners have exclusive rights to develop degraders for their selected and reserved targets. As a result, we are not permitted to pursue a target of potential interest – either alone or with another partner – while that target is bound by these restrictions.

Further, if our collaborations do not result in the successful development and commercialization of products or if one of our collaborators terminates its agreement with us or elects not to pursue a program within a collaboration, we may not receive any future research funding or milestone or royalty payments under that collaboration or in respect of that terminated program. If that were to happen, we might decide to abandon the program or to move the program forward on our own, which would require us to devote additional resources to the program on a going-forward basis. In addition, if one of our collaborators terminates its agreement with us generally, which they are permitted to do for convenience with between 90 and 270 days' notice, or with respect to a specific target or in connection with a material breach of the

agreement by us that remains uncured for a specified period of time, we may find it more difficult to attract new collaborators and our development programs may be delayed or the perception of us in the business and financial communities could be adversely affected. All of the risks relating to product development, marketing approval and commercialization described in this report apply to the activities of our collaborators.

It is also possible that our collaborators may not properly obtain, maintain, enforce, or defend the intellectual property or proprietary rights arising out of our licensed programs or may use our proprietary information in a way that could jeopardize or invalidate our proprietary information or expose us to potential litigation. For example, Roche, Biogen and Calico have the first right to enforce, and Roche also has the first right to defend, certain intellectual property rights under the applicable collaboration arrangement with respect to particular licensed programs and, although we may have the right to assume the enforcement and defense of these intellectual property rights if our collaborator does not, our ability to do so may be compromised by their actions. In addition, if any licensed program were later to revert to us, our ability to protect any intellectual property or other proprietary rights associated with that program would be impacted by the intellectual property filings made or other steps taken by our collaborator prior to program reversion. Further, our collaborators may own or co-own intellectual property covering our products that results from our collaborating with them and, in cases where that applies, we would not have the exclusive right to commercialize the collaboration intellectual property.

***We may form or seek collaborations or strategic alliances or enter into additional licensing arrangements in the future and we may not realize the benefits of those collaborations, alliances, or licensing arrangements.***

We may in the future form or seek strategic alliances, create joint ventures, or collaborations or enter into additional licensing arrangements with third parties that we believe will complement or augment our development and commercialization efforts with respect to our product candidates and any future product candidates that we may develop. Our likely collaborators in any other collaboration arrangements we may enter into include large and mid-size pharmaceutical companies and biotechnology companies. However, it is possible that we will not be able to enter into a collaboration agreement of this nature or that the terms of any potential new collaboration arrangement may not be favorable.

For example, we may seek to enter into collaboration arrangements to advance our CFT7455 product candidate in MM or other indications or we may form or seek to form collaboration arrangements to enable our development and commercialization of a product candidate in a specified geographic area. In addition, we may seek to enter into collaboration arrangements that enable other companies to access and leverage our TORPEDO platform to develop medicines directed at targets selected by our collaboration partners. Any of these relationships may require us to incur non-recurring and other charges, increase our near and long-term expenditures, issue securities that dilute our existing stockholders or disrupt our management and business.

In addition, we face significant competition in seeking appropriate strategic partners and the negotiation process for these sorts of transactions is time-consuming, complex and expensive. Moreover, we may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for our product candidates because they may be deemed to be at too early of a stage of development for collaborative effort and third parties may not view our product candidates as having the requisite potential to demonstrate safety and efficacy and obtain marketing approval. Additionally, our existing partners may decide to acquire or partner with other companies developing targeted protein degraders or directed at the targets or indications to which our product candidates are directed, which may have an adverse impact on our business prospects, financial condition and results of operations.

As a result, if we enter into additional collaboration agreements and strategic partnerships or license our product candidates, we may not be able to realize the benefit of those transactions if we are unable to successfully integrate them with our existing operations and company culture.

#### **Risks related to the commercialization of our product candidates**

***Even if any of our product candidates receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.***

If any of our product candidates receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. For example, current cancer treatments, such as chemotherapy and radiation therapy, are well-established in the medical community and doctors may continue to rely on these treatments. If our product candidates do not achieve an adequate level of acceptance, we may not generate

significant revenue from product sales and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and potential advantages compared to alternative treatments;
- the prevalence and severity of any side effects, in particular compared to alternative treatments;
- our ability to offer our products for sale at competitive prices;
- the convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians treating these patients to prescribe these therapies;
- the strength of marketing, sales and distribution support;
- the availability of third-party insurance coverage and adequate reimbursement;
- the timing of any marketing approval in relation to other product approvals;
- support from patient advocacy groups; and
- any restrictions on the use of our products together with other medications.

***As a company, we currently have no marketing and sales organization and no experience in marketing products. If we are unable to establish marketing and sales capabilities or enter into agreements with third parties to market and sell our product candidates, if approved, we may not be able to generate product revenue.***

As a company, we currently have no sales, marketing or distribution capabilities and no experience in marketing products. We intend to develop an in-house marketing organization and sales force, which will require significant capital expenditures, management resources and time. We will have to compete with other pharmaceutical and biotechnology companies to recruit, hire, train and retain marketing and sales personnel.

If we are unable or decide not to establish internal sales, marketing and distribution capabilities, we will pursue arrangements with third-party sales, marketing and distribution collaborators regarding the sales and marketing of our products, if approved. However, there can be no assurance that we will be able to establish or maintain these types of arrangements on favorable terms or if at all, or if we are able to do so, that these third-party arrangements will provide effective sales forces or marketing and distribution capabilities. Any revenue we receive will depend upon the efforts of these third parties, which may not be successful. We may have little or no control over the marketing and sales efforts of these third parties and our revenue from product sales may be lower than if we had commercialized our product candidates ourselves. We also face competition in our search for third parties to assist us with the sales and marketing efforts of our product candidates.

There can be no assurance that we will be able to develop in-house sales and distribution capabilities or establish or maintain relationships with third-party collaborators to commercialize any product in the United States or overseas.

***The market opportunities for our product candidates may be relatively small as we expect that they will initially be approved only for those patients who are ineligible for other approved treatments or have failed prior treatments. In addition, our estimates of the prevalence of our target patient populations may be inaccurate.***

Our product candidates may target cancer, but cancer therapies are sometimes characterized as first-line, second-line, third-line, or subsequent line and the FDA often approves new therapies initially only for a particular line of use. 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 – usually chemotherapy, antibody drugs, tumor-targeted small molecules, immunotherapy, hormone therapy, radiation therapy, surgery, other targeted therapies, or a combination of these therapies – proves unsuccessful, second-line therapy may be administered. Second-line therapies often consist of more chemotherapy, radiation, antibody drugs, tumor-targeted small molecules, or a combination of these. Third-line therapies can include chemotherapy, antibody drugs and small molecule tumor-targeted therapies, more invasive forms of surgery and new technologies. We expect initially to seek approval of our product candidates in most instances as a second- or third-line therapy, for use in patients with relapsed or refractory cancer. Subsequently, for those product candidates that prove to be sufficiently safe and beneficial, if any, we would expect to seek approval as a second-line therapy and potentially as a first-line therapy, but there is no guarantee that any of our product candidates, even if approved as a second- or third- or subsequent line of therapy, would subsequently be approved for an earlier line of therapy. Further, it is possible that, prior to getting any approvals for our product candidates in earlier lines of treatment, we might have to conduct additional clinical trials.

Our projections of both the number of people who have the cancers we are targeting, who may have their tumors genetically sequenced, as well as the subset of people with these cancers in a position to receive a particular line of therapy

and who have the potential to benefit from treatment with our product candidates, are based on our reasonable beliefs and estimates. These estimates have been derived from a variety of sources, including scientific literature, surveys of clinics, patient foundations, or market research and may prove to be incorrect or out of date. Further, new therapies may change the estimated incidence or prevalence of the cancers that we are targeting. Consequently, even if our product candidates are approved for a second- or third-line of therapy, the number of patients that may be eligible for treatment with our product candidates may turn out to be much lower than expected. In addition, we have not yet conducted market research to determine how treating physicians would expect to prescribe a product that is approved for multiple tumor types if there are different lines of approved therapies for each of those tumor types.

***Even if we receive marketing approval of any of our product candidates, our products may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, any of which would harm our business.***

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product candidate in a particular country but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, which would negatively impact the revenues, if any, we are able to generate from the sale of the product in that country. Adverse pricing limitations may, therefore, hinder our ability to recoup our investment in one or more of our product candidates, even if our product candidates obtain marketing approval.

Our ability to commercialize any product candidates successfully also will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government healthcare programs, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. The IRA's Medicare Drug Price Negotiation Program, administered by CMS, potentially may apply to our products, if they are selected for negotiation, which could materially reduce the amount of revenue we can generate from our products. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, government authorities and third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Coverage and reimbursement may not be available for any product that we commercialize and, even if these are available, the level of reimbursement may not be satisfactory. Reimbursement may affect the demand for, or the price of, any product candidate for which we obtain marketing approval. Obtaining and maintaining coverage and adequate reimbursement for our products may be difficult. We may be required to conduct expensive pharmacoeconomic studies to justify coverage and reimbursement or the level of reimbursement relative to other therapies. In addition, in light of the requirements of the IRA, we may be required to negotiate pricing for our product candidates, if approved, with Medicare, with those negotiated prices going into effect nine years after product approval. If coverage and adequate reimbursement are not available or reimbursement is available only to limited levels, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining coverage and reimbursement for newly approved drugs. In addition, coverage may be more limited than the purposes for which the drug is approved by the FDA or similar regulatory authorities outside of the United States. Moreover, eligibility for coverage and reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including research, development, intellectual property, manufacture, sale and distribution expenses. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States.

In the United States, no uniform policy for coverage and reimbursement for products exists among third-party payors. Therefore, coverage and reimbursement for our products can differ significantly from payor to payor. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the reimbursement rate that the payor will pay for the product. One payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product. Third-party payors may also limit coverage to specific products on an approved list, or formulary, which might not include all of the FDA-approved



products for a particular indication. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for any approved products that we develop could have an adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

***Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.***

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if or when we commercially sell any products that we may develop. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates or products that we may develop;
- termination of clinical trials;
- withdrawal of marketing approval, product recall, restriction on the approval or a “black box” warning or contraindication for an approved drug;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation and/or increased product liability insurance costs;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- injury to our reputation and significant negative media attention;
- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize any products that we may develop.

We currently maintain product liability insurance coverage to support our clinical development activities. We may need to purchase additional product liability insurance coverage as we expand our clinical trials and if and when we commence commercialization of our product candidates. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

**Risks related to our intellectual property**

***If we are unable to obtain and maintain patent protection for our technology, product candidates, and products or if the scope of the patent protection obtained is not sufficiently broad or enforceable, our competitors could develop and commercialize technology, product candidates, and products similar or identical to ours, our ability to successfully commercialize our technology, product candidates, and products may be impaired or we may not be able to compete effectively in our market.***

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect our intellectual property and prevent others from exploiting our platform technologies, our pipeline drug product candidates, any future drug product candidates we may develop and their use or manufacture.

Our commercial success depends in part on our ability to obtain and maintain patents and other proprietary protection in the United States and other countries with respect to our proprietary technology, product candidates, and products. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies and product candidates. Any disclosure to or misappropriation by third parties of our confidential proprietary information could enable competitors to quickly duplicate or surpass our technological achievements, thus eroding our competitive position in our market. Moreover, the patent applications we own, co-own or license may fail to result in issued patents in the United States or in other foreign countries.

The patent prosecution process is expensive and time consuming and we may not be able to file, prosecute, and maintain all necessary or desirable patent applications at a reasonable cost or in a timely manner. 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, we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents and patent applications, covering technology that we license from third parties or that we license to our collaborators. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

The patent position of the biopharmaceutical industry generally is highly uncertain, involves complex legal and factual questions and has been the subject of much litigation. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Publications of discoveries in the scientific literature often lag behind the actual discoveries and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our owned, co-owned or licensed patents or pending patent applications, or that we were the first inventors to file for patent protection of those inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights or those of our collaborators are highly uncertain. Our pending and future patent applications may not result in patents being issued that protect our technology, product candidates, or products, in whole or in part, or that effectively prevent others from commercializing competitive technologies, product candidates, and products. Changes in either the patent laws or interpretation of the patent or other laws in the United States and other countries may diminish the value of our patents and potential applications, narrow the scope of our patent protection, or cause us to be required to pay royalties to third parties. 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.

Our owned, co-owned and licensed patent estate consists principally of patent applications, many of which are at an early stage of prosecution. Even if our owned, co-owned and licensed patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned, co-owned or licensed patents by developing similar or alternative technologies, product candidates, or products in a non-infringing manner.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned, co-owned and licensed patents or patents obtained by our collaborators may be challenged in the courts or patent offices in the United States and abroad. These challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology, product candidates, and products or limit the duration of the patent protection of our technology, product candidates and products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting our drug product candidates might expire before or shortly after they are commercialized. As a result, our owned, co-owned and licensed patent portfolio, or that of our collaborators, may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

***Changes in patent laws or patent jurisprudence could diminish the value of our patents in general or increase third party challenges to our patents, thereby impairing our ability to protect our product candidates.***

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, or the Leahy-Smith Act, was signed into law and made a number of significant changes to U.S. patent law. These changes include provisions that affect the way patent applications are prosecuted and may also affect patent litigation. The U.S. Patent and Trademark Office, or the USPTO, developed new regulations and procedures to govern administration of the Leahy-Smith Act and many of the substantive changes to patent law associated with the Leahy-Smith Act, including the first-inventor-to-file provisions, became effective on March 16, 2013. The Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have an adverse effect on our business and financial condition. The first-to-file provision of the Leahy-Smith Act requires us to act promptly during the period from invention to filing of a patent application, as there is always a risk that a third party could file a patent application that could be blocking to our patent filings. However, even with the intention to act promptly, circumstances could prevent us from promptly filing or prosecuting patent applications on our inventions. The Leahy-Smith Act also enlarged the scope of disclosures that qualify as prior art, which can impact our ability to receive patent protection for an invention.

The Leahy-Smith Act created, for the first time, new procedures under which third parties may challenge issued patents in the United States, including post-grant review, *inter partes* review and derivations proceedings, all of which are adversarial proceedings conducted at the USPTO. Since the effectiveness of the Leahy-Smith Act, some third parties have been using these types of actions to seek and achieve the cancellation of selected or all claims of issued patents of their competitors. Under the Leahy-Smith Act, for a patent with a priority date of March 16, 2013 or later (which is the case for all of our patent filings), a third party can file a petition for post-grant review at any time during a nine-month window commencing at the time of issuance of the patent. In addition, for a patent with a priority date of March 16, 2013 or later, a third party can file a petition for *inter partes* review after the nine-month period for filing a post-grant review petition has expired. Post-grant review proceedings can be brought on any ground of challenge, whereas *inter partes* review proceedings can only be brought to raise a challenge based on published prior art. Under applicable law, the standard of review for these

types of adversarial actions at the USPTO are conducted without the presumption of validity afforded to U.S. patents, which is the standard that applies if a third party were to seek to invalidate a patent through a lawsuit filed in the federal courts of the United States. The USPTO issued a Final Rule on November 11, 2018 announcing that it will now use the same claim construction currently used in the federal courts of the United States—which is the plain and ordinary meaning of words used—to interpret patent claims in these USPTO proceedings. As a result of this regulatory landscape, if any of our patents are challenged by a third party in a USPTO proceeding of this nature, there is no guarantee that we will be successful in defending the challenged patent, which could result in our losing rights under the challenged patent in part or in whole.

As a result of this legislation, the issuance, scope, validity, enforceability and commercial value of our patent rights, or those of our collaborators, are highly uncertain, which could have an adverse effect on our business, financial condition, results of operations and prospects.

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

Competitors may infringe our issued patents, the patents of our licensors or collaborators or our other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive, time-consuming and unpredictable. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents. In addition, in a patent infringement proceeding, a court may decide that a patent of ours or our licensors or collaborators is invalid or unenforceable, in whole or in part, construe the patent's claims narrowly or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being or actually invalidated, held unenforceable or interpreted narrowly. Even if we successfully assert our patents, a court may not award remedies that sufficiently compensate us for our losses. In addition, we may not have sufficient financial or other resources to seek to enforce our patents adequately against perceived infringers, which could have a material and adverse effect on the profitability of our products.

***We may need to license intellectual property from third parties and licenses of this nature may not be available or may not be available on commercially reasonable terms.***

A third party may hold intellectual property, including patent rights, that are important or necessary to the development or manufacture of our products or our collaborators' products. It may, therefore, be necessary for us to use the patented or proprietary technology of a third party to commercialize our own technology or products or those of our collaborators, in which case we or our collaborators would be required to obtain a license from that third party. A license to that intellectual property may not be available or may not be available on commercially reasonable terms, which could have an adverse effect on our business and financial condition.

The licensing and acquisition of third-party intellectual property rights is a competitive practice. Companies that may be more established or have greater resources than we do may also be pursuing strategies to license or acquire third-party intellectual property rights that we may consider necessary or attractive in order to commercialize our product candidates. More established companies may have a competitive advantage over us due to their larger size and cash resources or greater clinical development and commercialization capabilities. We may not be able to successfully complete such negotiations and ultimately acquire the rights to the intellectual property surrounding the additional product candidates that we may seek to acquire.

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

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. There is considerable intellectual property litigation in the biopharmaceutical industry, as well as administrative proceedings for challenging patents, including reexamination, post-grant review, *inter partes* review, derivation proceedings, or interference proceedings before the USPTO and oppositions and other comparable proceedings in foreign jurisdictions.

We may become party to or threatened with future adversarial proceedings or litigation regarding intellectual property rights with respect to our product candidates and technology, including derivation, reexamination, post-grant review, *inter partes* review, or interference proceedings before the USPTO. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. As the bio-pharmaceutical industry expands and more patents are issued, the risk increases that our product candidates may give rise to claims of infringement of the patent rights of others. There may be third-party patents of which we are currently unaware with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our drug candidates. 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, third parties may obtain patents in the future and claim that our product candidates or use of our technologies infringes upon these patents.

If we are found by a court of competent jurisdiction to infringe a third party's intellectual property rights, we could be required to obtain a license from the applicable third-party intellectual property holder to continue developing and marketing our product candidates, products, and technology. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. We could be forced, including by court order, to cease commercializing the infringing technology or product. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

***A number of other companies, as well as universities and other organizations, file and obtain patents in the same areas as our products, which are targeted protein degraders, or our platform technologies and these patent filings could be asserted against us or our collaborators in the future, which could have an adverse effect on the success of our business and, if successful, could lead to expensive litigation that could affect the profitability of our products and/or prohibit the sale or use of our products.***

Our MonoDAC and BiDAC product candidates are small molecule pharmaceuticals, which degrade specific proteins. A number of companies and institutions have patent applications and issued patents in this general area, such as, for example, Accutar Biotechnology, Inc., Amgen Inc., Amphista Therapeutics, Ltd., Araxes Pharma, LLC, Arvinas, Inc., Astellas Pharma Inc., AstraZeneca PLC, Aurigen Discovery Technologies, Ltd., Bayer AG (and its subsidiary Vividion Therapeutics, Inc.), Beigene Co. Ltd., BioTheryX, Inc., Boehringer Ingelheim International GmbH, Bristol Myers Squibb Company (and its subsidiary Celgene Corporation), Captor Therapeutics, Inc., Cullgen, Inc., the Dana-Farber Cancer Institute and its Center for Protein Degradation, Dialectic Therapeutics, Inc., Foghorn Therapeutics, Inc., Frontier Medicines Corporation, GlaxoSmithKline PLC, Hinoa Pharmaceuticals, Inc., Janssen Biotech, Inc., Kymera Therapeutics, Inc., Monte Rosa Therapeutics, Inc., Novartis AG, Nurix Therapeutics, Inc., Otsuka Pharmaceuticals, Inc., Phoremest, Ltd., Prelude Therapeutics, Inc., Proteovant Therapeutics, Inc., Roche AG, Salaris Pharmaceuticals Inc., Seed Therapeutics, Inc., Sichuan Haisco Pharmaceutical Co., Ltd., the University of Michigan School of Medicine, Vertex Pharmaceuticals, Inc., and others. If any of these companies or institutions or others not included in this list were to assert that one of its patents is infringed by any product candidate or product we might develop or its use or manufacture, we or our collaborators may be drawn into expensive litigation, which could adversely affect our business prospects, financial condition and results of operations, require extensive time from and cause the distraction of members of our management team and employees at large. Further, if litigation of this nature were successful, that could have a material and adverse effect on the profitability of our products or prohibit their sale. We may not be aware of patent claims that are currently or may in the future be pending that could affect our business or products. Patent applications are typically published between six and eighteen months from filing and the presentation of new claims in already pending applications can sometimes not be visible to the public, which would include us, for a period of time. In addition, even after a patent application is publicly available, we may not yet have seen that patent application and may, therefore, not be aware of the claims or scope of filed and published patent applications. As a result, we cannot provide any assurance that a third party practicing in the general area of our technology will not present or has not presented a patent claim that covers one or more of our product candidates or products or their methods of use or manufacture. If that were to occur, we or our collaborators, as applicable, may have to take steps to try to invalidate the applicable patent or application and, in a situation of that nature, we or our collaborators may either choose not to do so or our attempt may not be successful. If we determine that we require a license to a third party's patent or patent application, we may discover that a license may not be available on reasonable terms, or at all, which could prevent us or our collaborators from selling a product or using our proprietary technologies.

***Our products are subject to The Drug Price Competition and Patent Term Restoration Act of 1984, which is also referred to as the Hatch-Waxman Act, in the United States, which can increase the risk of litigation with generic companies trying to sell our products and may cause us to lose patent protection.***

Because our clinical candidates are pharmaceutical molecules that will be reviewed by the Center for Drug Evaluation and Research of the FDA, after commercialization they will be subject in the United States to the patent litigation process of the Hatch-Waxman Act, as amended to date, which allows a generic company to submit an Abbreviated New Drug Application, or ANDA, to the FDA to obtain approval to sell a generic version of our drug using bioequivalence data only. Under the Hatch-Waxman Act, we will list patents that cover our drug products or their respective methods of use in the FDA's compendium of "Approved Drug Products with Therapeutic Equivalence Evaluation," sometimes referred to as the FDA's Orange Book.

There are detailed rules and requirements regarding the patents that may be submitted to the FDA for listing in the Orange Book. We may be unable to obtain patents covering our product candidates that contain one or more claims that satisfy the requirements for listing in the Orange Book. Even if we submit a patent for listing in the Orange Book, the FDA may decline to list the patent or a generic drug manufacturer may challenge the listing. If one of our product candidates is approved and a patent covering that product candidate is not listed in the Orange Book, with respect to any unlisted patent, a generic drug manufacturer would not have to provide advance notice to us of any ANDA filed with the FDA to obtain permission to sell a generic version of that product candidate.

Currently, in the United States, the FDA may grant five years of data exclusivity for new chemical entities, or NCEs, which are drugs that contain no active portion that has been approved by the FDA in any other new drug application, or NDA. We expect that all of our products will qualify as NCEs; however, the FDA will not conduct an assessment for NCE status until it is reviewing a marketing application for that drug. A generic company can submit an ANDA to the FDA four years after approval of any of our drug products designated as an NCE. The submission of an ANDA by a generic company is considered a technical act of patent infringement. The generic company can certify that it will wait until the natural expiration date of our listed patents to sell a generic version of our product or can certify that one or more of our listed patents are invalid, unenforceable or not infringed. If the generic manufacturer elects the latter, we will have 45 days to bring a patent infringement lawsuit against the generic company. If we were to do so, that would likely initiate a challenge to one or more of our Orange Book listed patents based on arguments from the generic manufacturer that our listed patents are invalid, unenforceable or not infringed. If a lawsuit is brought, the FDA is prevented from issuing a final approval of an ANDA for the generic drug until 30 months from our receipt of the generic manufacturer's certification notice, or such shorter or longer time as the presiding court might order based on certain behaviors of the parties or a final decision of a court holding that our asserted patent claims are invalid, unenforceable or not infringed. If we do not properly list our relevant patents in the Orange Book or if we fail to file a lawsuit in response to a certification from a generic company under an ANDA in a timely manner, or if we do not prevail in the resulting patent litigation, we can lose our ability to benefit from a proprietary market based on patent protection covering our drug products and we may find that physicians will switch to prescribing and dispensing generic versions of our drug products. Further, even if we were to list our relevant patents in the Orange Book correctly, bring a lawsuit in a timely manner, and prevail in that lawsuit, the generic litigation may come at a significant cost to us, both in terms of attorneys' fees and employee time and distraction over a long period. Further, it is common for more than one generic company to try to sell an innovator's drug at the same time and, as a result, we may face the cost and distraction of multiple lawsuits from generic manufacturers at the same time. We may also determine that it is necessary to settle these types of lawsuits in a manner that allows the generic company to enter our market prior to the expiration of our patent or otherwise in a manner that adversely affects the strength, validity or enforceability of our patents.

***A number of pharmaceutical companies have been the subject of intense review by the U.S. Federal Trade Commission or a corresponding agency in another country based on how they have conducted or settled patent litigation related to pharmaceutical products. In fact, certain reviews have led to an allegation of an anti-trust violation, sometimes resulting in a fine or loss of rights. We cannot be sure that we would not also be subject to a review of this nature or that the result of a review of this nature would be favorable to us, or that any review of this nature would not result in a fine or penalty.***

The U.S. Federal Trade Commission, or FTC, has brought a number of lawsuits in federal court in the past few years to challenge ANDA litigation settlements reached between innovator companies and generic companies as anti-competitive. As an example, the FTC has taken an aggressive position that anything of value is a payment, whether money is paid or not. Under their approach, if an innovator, as part of a patent settlement, agrees not to launch or delay its launch of an authorized generic during the 180-day period granted to the first generic company to challenge an Orange Book listed patent covering an innovator drug, or negotiates a delay in entry without payment, the FTC may consider it an unacceptable reverse payment. Companies in the pharmaceutical industry have argued that these types of agreements are rational business decisions entered into by drug innovators as a way to address risk and that these settlements should, therefore, be immune from antitrust attack if the terms of the settlement are within the scope of the exclusionary potential of the patent. In 2013, the U.S. Supreme Court in a five-to-three decision in *FTC v. Actavis, Inc.* rejected both the pharmaceutical industry's and FTC's arguments with regard to so-called reverse payments. Instead, the Supreme Court held that whether a "reverse payment" settlement involving the exchange of consideration for a delay in entry is subject to an anti-competitive analysis depends on five considerations: (a) the potential for genuine adverse effects on competition; (b) the justification of payment; (c) the patentee's ability to bring about anti-competitive harm; (d) whether the size of the payment is a workable surrogate for the patent's weakness; and (e) that antitrust liability for large unjustified payments does not prevent litigating parties from settling their lawsuits, for example, by allowing the generic drug to enter the market before the patent expires on the branded drug without the patentee paying the generic manufacturer. Further, whether a reverse payment is justified depends upon its size, scale in relation to the patentee's anticipated future litigation costs, and independence from other services for which it might represent payment (as was the case in *Actavis*), as well as the lack of any other convincing

justification. The Supreme Court instead held that reverse payment settlements can potentially violate antitrust laws and are subject to the standard antitrust rule-of-reason analysis, with the burden of proving that an agreement is unlawful on the FTC. In reaching this decision, the Supreme Court left to the lower courts the structuring of this rule of reason analysis.

If we are faced with drug patent litigation, including Hatch-Waxman litigation with a generic company, we could be faced with an FTC challenge of this nature, which challenge could impact how or whether we settle the case and, even if we strongly disagree with the FTC's position, we could face a significant expense or penalty. Any litigation settlements we enter into with generic companies under the Hatch-Waxman Act could also be challenged by third-party payors such as insurance companies, direct purchasers or others who consider themselves adversely affected by the settlement. These kinds of follow-on lawsuits, which may be class action suits, can be expensive and can continue over multiple years. If we were to face lawsuits of this nature, we may not be successful in defeating these claims and we may, therefore, be subject to large payment obligations, which we may not be able to satisfy in whole or in part.

***We may not be able to obtain patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984 in the United States and, as a result, our product candidates, if approved, may not have patent protection for a sufficient period.***

In the United States, the Drug Price Competition and Patent Term Restoration Act of 1984 permits one patent term extension of up to five years beyond the normal expiration of one patent per product, which if related to a method of treatment patent, is limited to the approved indication. The length of the patent term extension is typically calculated as one-half of the clinical trial period plus the entire period of time during the review of the NDA by the FDA, minus any time of delay by us during these periods. There is also a limit on the patent term extension to a term that is no greater than fourteen years from the date of drug approval. Therefore, if we select and are granted a patent term extension on a recently filed and issued patent, we may not receive the full benefit of a possible patent term extension, if at all. We might also not be granted a patent term extension at all, because of, for example, our failure to apply within the applicable period, failure to apply prior to the expiration of relevant patents or other failure to satisfy any of the numerous applicable requirements. In addition, the regulatory review period of an FDA-approved product may not serve as the basis for a patent term extension if the active ingredient of such product was subject to regulatory review and approval in an earlier product approved by the FDA. Moreover, the applicable authorities, including the FDA and the USPTO in the United States and any equivalent regulatory authority in other countries, may not agree with our assessment of whether extensions of this nature are available and may refuse to grant extensions to our patents or may grant more limited extensions than we request. If this occurs, our competitors may be able to obtain approval of competing products following our patent expiration by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case. If this were to occur, it could have an adverse effect on our ability to generate product revenue.

In Europe, supplementary protection certificates are available to extend a patent term up to five years to compensate for patent term lost during regulatory review, and this period can be extended to five and a half years if data from clinical trials is obtained in accordance with an agreed Pediatric Investigation Plan. Although all countries in Europe must provide supplementary protection certificates, there is no unified legislation among European countries and, as a result, drug developers must apply for supplementary protection certificates on a country-by-country basis. As a result, a company may need to expend significant resources to apply for and receive these certificates in all relevant countries and may receive them in some, but not all, countries, if at all.

***Weakening patent laws and enforcement by courts in the United States and foreign countries may impact our ability to protect our markets.***

The U.S. Supreme Court has issued opinions in patent cases in the last few years that many consider may weaken patent protection in the United States, either by narrowing the scope of patent protection available in certain circumstances, holding that certain kinds of innovations are not patentable or generally otherwise making it easier to invalidate patents in court. Additionally, there have been recent proposals for additional changes to the patent laws of the United States and other countries that, if adopted, could impact our ability to obtain patent protection for our proprietary technology or our ability to enforce our proprietary technology. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO, and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

The laws of some foreign jurisdictions do not protect intellectual property rights to the same extent as in the United States and many companies have encountered significant difficulties in protecting and defending such rights in foreign jurisdictions. If we encounter such difficulties in protecting or are otherwise precluded from effectively protecting our intellectual property rights in foreign jurisdictions, our business prospects could be substantially harmed. For example, we could become a party to foreign opposition proceedings, such as at the European Patent Office, or patent litigation and other proceedings in a foreign court. If so, uncertainties resulting from the initiation and continuation of such proceedings

could have an adverse effect on our ability to compete in the marketplace. The cost of foreign adversarial proceedings can also be substantial, and in many foreign jurisdictions, the losing party must pay the attorney fees of the winning party.

***We may be subject to claims by third parties asserting that we, our employees, consultants or contractors have misappropriated the applicable third party's intellectual property or claiming ownership of what we regard as our own intellectual property.***

We employ individuals who were previously employed at universities as well as other biotechnology or pharmaceutical companies, including our competitors or potential competitors. We have received confidential and proprietary information from collaborators, prospective licensees, and other third parties that may be subject to contractual confidentiality and non-use obligations. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these employees or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. We may also be subject to claims that former employers or other third parties have an ownership interest in our patents. Litigation may be necessary to defend against these claims. We may not be successful in defending these claims, and if we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of or right to use valuable intellectual property. Even if we are successful, litigation could result in substantial cost and reputational loss and be a distraction to our management and other employees.

In addition, while it is our policy to require our employees, consultants, and contractors who may be involved in the development of intellectual property to execute agreements assigning any resulting intellectual property to us, we may be unsuccessful in executing an agreement to that effect with each party who in fact develops intellectual property that we regard as our own. Assignment agreements of this nature may not be self-executing or may be breached and we may be forced to bring claims against third parties or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property. In addition, an employee or contractor could create an invention but not inform us of it, in which case we could lose the benefit of the invention and the employee or contractor may leave to develop the invention elsewhere.

***Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.***

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims 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. Litigation or proceedings of this nature 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 litigation or proceedings of this nature 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.

***Obtaining and maintaining patent protection depends on compliance with various procedural, documentary, fee payment, and other requirements imposed by governmental patent offices and the protection of our patents could be reduced or eliminated if we fail to comply with these requirements.***

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and patent offices in foreign countries in several stages over the lifetime of a patent application and any resulting patent. The USPTO and patent offices in foreign countries require compliance with many procedural, documentary, fee payment, and other requirements during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of a patent or patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees, and failure to properly legalize and submit formal documents. In such an event, our competitors might be able to enter the market, which would have an adverse effect on our business.

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

In addition to seeking patents for some of our technology and product candidates, we also rely on trade secrets, including unpatented know-how, technology, and other proprietary information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have

access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors, and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. These agreements may not effectively prevent disclosure of confidential information nor result in the effective assignment to us of intellectual property and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information or other breaches of the agreements. In addition, others may independently discover our trade secrets and proprietary information. In that case, we could not assert any trade secret rights against that third party. Despite these efforts, 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 of a dispute of this nature is inherently unpredictable. Costly and time-consuming litigation could be necessary to seek to enforce and determine the scope of our proprietary rights, and our failure to obtain or maintain trade secret protection could adversely affect our competitive business position. In addition, some courts outside of the United States are less willing or unwilling to protect trade secrets. The Defend Trade Secrets Act of 2016 is a U.S. federal law that allows an owner of a trade secret to sue in federal court when its trade secret has been misappropriated. Congress passed this law in an attempt to strengthen the rights of trade secret owners whose valuable assets are taken without authorization. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate them, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

***We only have limited geographical protection with respect to certain of our patents and we may not be able to protect our intellectual property rights throughout the world.***

Filing, prosecuting, maintaining, and defending patents covering our product candidates in all countries throughout the world would be prohibitively expensive. As a result, our intellectual property rights in some countries outside the United States can be less extensive than the protection we might have in the United States. In-licensing patents covering our product candidates in all countries throughout the world may similarly be prohibitively expensive, if these in-licensing opportunities are available to us at all. Further, in-licensing or filing, prosecuting, maintaining, and defending patents even in only those jurisdictions in which we develop or commercialize our product candidates may be prohibitively expensive or impractical. Competitors may use our and our licensors' technologies in jurisdictions where we have not obtained patent protection or licensed patents to develop their own products and, further, may export otherwise infringing products to territories where we and our licensors have patent protection, but enforcement is not as strong as that in the United States or the European Union. These products may compete with our product candidates, and our or our licensors' patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

In addition, we may decide to abandon national and regional patent applications while they are still pending. The grant proceeding of each national or regional patent is an independent proceeding that may lead to situations in which applications may be rejected by the relevant patent office, while substantively similar applications are granted by others. For example, relative to other countries, China has a heightened detailed description requirement for patentability. Further, generic drug manufacturers or other competitors may challenge the scope, validity or enforceability of our or our licensors' patents, requiring us or our licensors to engage in complex, lengthy, and costly litigation or other proceedings. Generic drug manufacturers may develop, seek approval for and launch generic versions of our products. It is also quite common that depending on the country, the scope of patent protection may vary for the same product candidate or technology.

The laws of some jurisdictions do not protect intellectual property rights to the same extent as the laws or regulations in the United States and the European Union, and many companies have encountered significant difficulties in protecting and defending proprietary rights in such jurisdictions. Moreover, the legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets or other forms of intellectual property, which could make it difficult for us to prevent competitors in some jurisdictions from marketing competing products in violation of our proprietary rights generally.

Proceedings to enforce our patent rights in foreign jurisdictions, whether or not successful, are likely to result in substantial costs and divert our efforts and attention from other aspects of our business, and could additionally put our or our licensors' patents at risk of being invalidated or interpreted narrowly, could increase the risk of our or our licensors' patent applications not issuing or could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, while damages or other remedies may be awarded to the adverse party, which may be commercially significant. If we prevail, damages or other remedies awarded to us, 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. Further, while we intend to protect our intellectual property rights in our expected significant markets, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our product candidates. Accordingly, our efforts to protect our



intellectual property rights in these countries may be inadequate, which may have an adverse effect on our ability to successfully commercialize our product candidates in all of our expected significant foreign markets. If we or our licensors encounter difficulties in protecting or are otherwise precluded from effectively protecting the intellectual property rights important for our business in such jurisdictions, the value of these rights may be diminished and we may face additional competition in those jurisdictions.

In some jurisdictions, compulsory licensing laws compel patent owners to grant licenses to third parties. In addition, some countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors are forced to grant a license to third parties under patents relevant to our business, or if we or our licensors are prevented from enforcing patent rights against third parties, our competitive position may be substantially impaired in such jurisdictions.

#### **Risks related to regulatory matters**

***Receiving regulatory approval from the FDA and foreign regulatory authorities is lengthy, time-consuming, and inherently unpredictable and, if we are ultimately unable to obtain marketing approval for our product candidates, our business will be substantially harmed.***

The amount of time required to obtain approval by the FDA and foreign regulatory authorities is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval standards, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. We have not obtained marketing approval for any product candidate, and it is possible that none of our existing product candidates, or any product candidates we may seek to develop in the future (independently or with one of our collaboration partners), will ever obtain marketing approval.

Our product candidates could fail to receive marketing approval for many reasons, including the following:

- the FDA or foreign regulatory authority, each referred to here as a health authority, may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the health authority that a product candidate is safe and effective for its proposed indication, or that it is of sufficient strength, identity, or quality in accordance with the health authority's standards;
- results of clinical trials may not meet the level of statistical significance required by the health authority for approval;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the health authority may disagree with our interpretation of data from preclinical studies or clinical trials;
- data collected from clinical trials of our product candidates may not be sufficient valid or of sufficient quality to support the submission of an NDA to the FDA or other submission to a foreign regulatory authority or to obtain marketing approval in the United States or any other country or jurisdiction;
- the health authority may find deficiencies with or fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and
- the approval standards, policies, or regulations of a health authority may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy drug development process, as well as the unpredictability of future clinical trial results, may result in our failing to obtain regulatory approval to allow us to market any of our product candidates, which would significantly harm our business, results of operations, and prospects. The FDA and other health authorities have substantial discretion in the approval process and determining when or whether regulatory approval will be obtained for any of our product candidates, including in the context of accelerated approvals. Even if we believe the data collected from clinical trials of our product candidates are promising, that data may not be sufficient to support approval by the FDA or any other health authority.

In addition, even if we were to obtain approval, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may not approve the price we intend to charge for our products, may grant approval contingent on the performance of costly post-marketing clinical trials or may approve a product candidate with a label that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

***Even if we obtain FDA approval for any of our product candidates in the United States, we may never obtain approval for or commercialize any of them in any other jurisdiction, which would limit our ability to realize their full market potential.***

In order to market any products in any particular jurisdiction, we must establish and comply with numerous and varying regulatory requirements on a country-by-country basis regarding safety and efficacy.

Approval by the FDA in the United States does not ensure approval by regulatory authorities in other countries or jurisdictions. However, the failure to obtain approval in one jurisdiction may negatively impact our ability to obtain approval elsewhere. In addition, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries and regulatory approval in one country does not guarantee regulatory approval in any other country.

Approval processes vary among countries and can involve additional product testing and validation, and additional administrative review periods. Seeking foreign regulatory approval could result in difficulties and increased costs for us and require additional preclinical studies or clinical trials, which could be costly and time consuming. Regulatory requirements can vary widely from country to country and could delay or prevent the introduction of our products in those countries. We do not have any product candidates approved for sale in any jurisdiction, including in international markets, and we do not have experience as a company in obtaining regulatory approval in international markets. If we fail to comply with regulatory requirements in international markets or to obtain and maintain required approvals, or if regulatory approvals in international markets are delayed, our target market will be reduced and our ability to realize the full market potential of any product we develop will be unrealized.

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

If any of our product candidates are approved, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies, and submission of safety, efficacy and other post-market information, including both federal and state requirements in the United States, and requirements of comparable foreign regulatory authorities. In addition, we will be subject to continued compliance with cGMP and GCP requirements for any clinical trials that we conduct post-approval.

Manufacturers and manufacturers' facilities are required to comply with extensive FDA and comparable foreign regulatory authority requirements, including ensuring that quality control and manufacturing procedures conform to cGMP regulations and applicable product tracking and tracing requirements. As such, we and our CMOs will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any NDA, other marketing application, and previous responses to inspection observations. Accordingly, we and others with whom we work must continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, and quality control.

Any regulatory approvals that we receive for our product candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials and surveillance to monitor the safety and efficacy of the product candidate. The FDA may also require a REMS program as a condition of approval of our product candidates, which could entail requirements for long-term patient follow-up, 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. Comparable foreign regulatory authorities may also have programs similar to REMS. In addition, if the FDA or a comparable foreign regulatory authority approves our product candidates, we will have to comply with requirements including submissions of safety and other post-marketing information and reports and registration.

The FDA may impose consent decrees or 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 our product candidates, including adverse events of unanticipated severity or frequency, or with our third-party CMOs or manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, 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;
- fines, warning 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 license approvals;
- product seizure or detention or refusal to permit the import or export of our product candidates; and
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising, and promotion of products that are placed on the market. Products may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses and a company that is found to have improperly promoted off-label uses may be subject to significant liability. However, physicians may, in their independent medical judgment, prescribe legally available products for off-label uses. The FDA does not regulate the behavior of physicians in their choice of treatments, but the FDA does restrict manufacturers' communications on the subject of off-label use of their products. The policies of the FDA and of comparable foreign regulatory authorities may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

***A Breakthrough Therapy designation by the FDA, even if granted for any of our product candidates, may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that our product candidates will receive marketing approval.***

We may seek Breakthrough Therapy designation for our CFT7455 and CFT8634 product candidates, and some or all of our future product candidates. A Breakthrough Therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For product candidates that have been designated as Breakthrough Therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Drugs designated as breakthrough therapies by the FDA may also be eligible for other expedited approval programs, including accelerated approval.

Designation as a Breakthrough Therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a Breakthrough Therapy, the FDA may disagree and instead determine not to make such a designation. In any event, although Breakthrough Therapy designation is designed to expedite the development and review of drugs that receive such designation, the receipt of a Breakthrough Therapy designation for a product candidate may not result in a faster development process, review or approval compared to candidate products considered for approval under non-expedited FDA review procedures and does not assure ultimate approval by the FDA of a product candidate. In addition, even if one or more of our product candidates qualify as Breakthrough Therapies, the FDA may later decide that the product no longer meets the conditions for qualification. Thus, even though we intend to seek Breakthrough Therapy designation for our lead product candidates and some or all of our future product candidates for the treatment of various cancers, there can be no assurance that we will receive Breakthrough Therapy designations.

***A Fast Track designation by the FDA, even if granted for one or all of our lead product candidates, or any of our other current or future product candidates, may not lead to a faster development or regulatory review or approval process, and does not increase the likelihood that our product candidates will receive marketing approval.***

At various times, we may seek Fast Track designation for one or more of our product candidates. If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, the drug sponsor may apply for FDA Fast Track designation for a particular indication. We may seek Fast Track designation for one or all of our lead product candidates and/or certain of our future product candidates, but there is no assurance that the FDA will grant this status to any of our proposed product candidates and we might only be successful in receiving a Fast Track designation from the FDA for a product candidate after applying on more than one occasion. Marketing applications filed by sponsors of products in Fast Track development may qualify for priority review under the policies and procedures offered by the FDA, but the receipt of a Fast Track designation does not assure any such qualification or ultimate marketing approval by the FDA. The FDA has broad discretion whether or not to grant a Fast Track designation, so even if we believe a particular product candidate is eligible for this designation, there can be no assurance that the FDA would decide to grant it. Even if we do receive a Fast Track designation, and even though Fast

Track designation is designed to expedite the development and review of drugs that receive such designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures, and receiving a Fast Track designation does not provide assurance of ultimate FDA approval. In addition, the FDA may withdraw a Fast Track designation if it believes that the designation is no longer supported by data from our clinical development program. In addition, the FDA may withdraw any Fast Track designation at any time.

***We have obtained Orphan Drug Designation for CFT7455 and CFT8634, and if we decide to seek Orphan Drug Designation for any other current or future product candidates, we may be unsuccessful or may be unable to maintain the benefits associated with Orphan Drug Designation, including the potential for supplemental market exclusivity.***

In August 2021, the FDA granted Orphan Drug Designation to CFT7455 for the treatment of MM, and in March 2022, the FDA granted Orphan Drug Designation to CFT8634 for the treatment of soft tissue sarcoma. We may seek Orphan Drug Designation for one or more of our other current or future product candidates. Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may grant an Orphan Drug Designation to a drug intended to treat a rare disease or condition, defined as a disease or condition with a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States 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. In the United States, receipt of an Orphan Drug Designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages, and user-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. Although Orphan Drug Designation is intended to incent drug development for rare diseases or conditions, Orphan Drug Designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

If a product that has an Orphan Drug Designation subsequently receives the first FDA approval for a particular active ingredient for the disease 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 an NDA, to market the same drug for the same indication for seven years, 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. As a result, even if one of our product candidates receives orphan drug exclusivity, the FDA can still approve other drugs that have a different active ingredient for use in treating the same indication or disease. Further, the FDA can waive orphan drug exclusivity if we are unable to manufacture sufficient supply of our product.

We may also seek Orphan Drug Designations for our other lead candidates and/or some or all of our other current or future product candidates in additional orphan indications in which there is a medically plausible basis for the use of these product candidates. Even when we obtain an Orphan Drug Designation, exclusive marketing rights in the United States may be limited if we 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 or if we, through our manufacturer, are unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. In addition, even if we seek Orphan Drug Designation for other product candidates, we may never receive these designations. For example, the FDA has expressed concerns regarding the regulatory considerations for Orphan Drug Designation as applied to tissue agnostic therapies and the FDA may interpret the FDCA and its orphan drug regulations, in a way that limits or blocks our ability to obtain an Orphan Drug Designation or orphan drug exclusivity, if our product candidates are approved, for our targeted indications.

***We may seek approval of our product candidates, where applicable under the FDA's accelerated approval pathway. This pathway may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that our product candidates will receive marketing approval.***

We plan to seek accelerated approval of our lead product candidates and may seek approval of future product candidates, where applicable, using the FDA's accelerated approval pathway. A product may be eligible for accelerated approval if it treats a serious or life-threatening condition and generally provides a meaningful advantage over available therapies. In addition, it must demonstrate an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, or IMM, that is reasonably likely to predict an effect on IMM or other clinical benefit. Under FDORA, the FDA is permitted to require, as appropriate, that a post-approval confirmatory study or studies be underway prior to approval or within a specified time period after the date of approval for a product that is granted accelerated approval. FDORA also requires sponsors to send updates to the FDA every 180 days on the status of such studies, including progress toward enrollment targets, and the FDA must promptly post this information publicly. FDORA also gives the FDA increased authority to withdraw accelerated approval on an expedited basis if the sponsor fails to conduct such studies in a timely manner, send the necessary updates to the FDA, or if such post-approval studies fail to verify the drug's predicted clinical benefit; and to take action, such as issuing fines,

against companies that fail to conduct with due diligence any post-approval confirmatory study or submit timely reports to the agency on their progress. In addition, the FDA generally requires pre-approval of promotional materials for products receiving accelerated approval, which could adversely impact the timing of the commercial launch of the product. Thus, even if we seek to utilize the accelerated approval pathway for any of our product candidates, we may not be able to obtain accelerated approval, and even if we do, that product may not experience a faster development or regulatory review or approval process. In addition, receiving accelerated approval does not assure the product's accelerated approval will eventually be converted to a traditional approval.

***The FDA may identify in a written request that pediatric information would be beneficial for a product candidate for which we obtained approval and request that we conduct pediatric studies. We may elect not to perform these studies or, if we opted to conduct these studies, we may not be able to complete them or the data generated from these studies may not be acceptable to the FDA.***

Section 505(A) of the Food, Drug, and Cosmetic Act, or the FDC Act, provides incentives to drug manufacturers who conduct studies of drugs in children. Referred to as the "pediatric exclusivity provision," this law provides an additional six months of non-patent exclusivity to pharmaceutical manufacturers that conduct acceptable pediatric studies of new and currently-marketed drug products for which pediatric data would be beneficial pursuant to a written request by the FDA. As a result, if we received a written request for pediatric studies from the FDA, conducted pediatric clinical studies and submitted reports that were accepted by the FDA within the statutory time limits, we could receive an additional six-months of regulatory exclusivity beyond all other types of patent and non-patent exclusivity then in effect for all our approved drug products that contain the active moiety for which pediatric exclusivity was granted. However, even if we received a written request for pediatric studies from the FDA for one or more of our drug products, we may determine not to or be unable to carry out pediatric studies that comply with Section 505(A) of the FDC Act, or we may carry out studies that are not accepted by the FDA for this purpose. If this situation were to arise, we would not receive this additional six-month regulatory exclusivity extension.

***Our relationships with customers, healthcare providers, and third-party payors are or will be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, health information privacy and security laws, and other healthcare laws and regulations. If we are unable to comply or have not fully complied with these laws, we could face substantial penalties.***

Healthcare providers and third-party payors in the United States and elsewhere will play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our current and future arrangements with healthcare professionals, principal investigators, consultants, customers, and third-party payors subject us to various federal and state fraud and abuse laws and other healthcare laws that may constrain the business or financial arrangements and relationships through which we research, sell, market, and distribute our product candidates, if we obtain marketing approval. In particular, the research of our product candidates, as well as the promotion, sales, and marketing of healthcare items and services, as well as certain business arrangements in the healthcare industry, are subject to extensive laws designed to: (i) prevent fraud, kickbacks, self-dealing, and other abusive practices, (ii) guarantee the security and privacy of health information, and (iii) increase transparency around the financial relationships between physicians, teaching hospitals, and manufacturers of drugs, medical devices, and biologics. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, structuring and commission(s), certain customer incentive programs, and other business or financial arrangements. See the sections entitled "*Business — Other Healthcare Laws*" and "*Business — Healthcare Reform*" included above in this filing.

Ensuring that our business arrangements and practices with third parties comply with applicable healthcare laws and regulations will likely be costly. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from participating in government funded healthcare programs such as Medicare and Medicaid, 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, contractual damages, reputational harm, and the curtailment or restructuring of our operations. The shifting compliance environment and the need to build and maintain robust and expandable systems to comply with multiple jurisdictions with different compliance or reporting requirements increases the possibility that a healthcare company may run afoul of one or more of the requirements.

If the physicians or other providers or entities with whom we expect to do business are found not to comply with applicable laws, they may be subject to significant criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs. Even if resolved in our favor, litigation or other legal proceedings relating to healthcare laws and regulations 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. 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. Litigation or proceedings of this nature could substantially increase our operating losses and reduce the resources available for development, manufacturing, sales, marketing or distribution activities. Uncertainties resulting from the initiation and continuation of litigation or other proceedings relating to applicable healthcare laws and regulations could have an adverse effect on our ability to compete in the marketplace.

***The successful commercialization of our product candidates in the United States and abroad will depend in part on the extent to which third-party payors, including governmental authorities and private health insurers, provide coverage and adequate reimbursement levels, as well as implement pricing policies favorable for our product candidates. Failure to obtain or maintain coverage and adequate reimbursement for our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue.***

Significant uncertainty exists as to the coverage and reimbursement status of any products for which we may obtain regulatory approval. In the United States and in other countries, patients who are provided medical treatment for their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. The availability of coverage and adequacy of reimbursement for our products by third-party payors, including government health care programs (e.g., Medicare, Medicaid or TRICARE in the United States), managed care providers, private health insurers, health maintenance organizations, and other organizations is essential for most patients to be able to afford medical services and pharmaceutical products such as our product candidates. Third-party payors decide which medications they will pay for and establish reimbursement levels. See the section entitled “*Business — Coverage and Reimbursement*” included above in this filing.

Our ability to successfully commercialize our product candidates will depend in part on the extent to which coverage and adequate reimbursement for our products and related treatments will be available from third-party payors. Moreover, a payor’s decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. If coverage and adequate reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment. A decision by a third-party payor not to cover or not to separately reimburse for our medical products or therapies using our products could reduce physician utilization of our products once approved.

We cannot be sure that coverage and reimbursement in the United States and other countries will be available for our current or future product candidates or for any procedures using our current or future product candidates, and any reimbursement that may become available may not be adequate or may be decreased or eliminated in the future. In the United States, no uniform policy for coverage and reimbursement for products exists among third-party payors. Therefore, coverage and reimbursement for our products can differ significantly from payor to payor. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the reimbursement rate that the payor will pay for the product. One payor’s determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product. Third-party payors may also limit coverage to specific products on an approved list, or formulary, which might not include all of the FDA-approved products for a particular indication. The principal decisions about reimbursement for new medicines in the United States are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the United States Department of Health and Human Services, or HHS. CMS will decide whether and to what extent our products will be covered and reimbursed under Medicare and private payors tend to follow CMS to a substantial degree. Factors considered by payors in determining reimbursement are based on whether the product is:

- a covered benefit under its health plan;
- safe, effective, and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

We cannot be sure that coverage and reimbursement will be available for or accurately estimate the potential revenue from our product candidates or assure that coverage and reimbursement will be available for any product that we may develop.

Further, increasing efforts by third-party payors in the United States and abroad to cap or reduce healthcare costs may cause payor 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 product candidates. In order to secure coverage and

reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain FDA or comparable regulatory approvals. Additionally, we may also need to provide discounts to purchasers, private health plans or government healthcare programs. Our product candidates may nonetheless not be considered medically necessary or cost-effective. If third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover the product after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to sell its products at a profit. We expect to experience pricing pressures from third-party payors in connection with the potential sale of any of our product candidates.

Lastly, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, countries in the European Union, or EU, Member States can restrict the range of medicinal products for which their national health insurance systems provide reimbursement and they can control the prices of medicinal products for human use. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost effectiveness of a particular product candidate to currently available therapies. An EU Member State may approve a specific price for the medicinal product, or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. Approaches between EU Member States are diverging. For example, in France, effective market access will be supported by agreements with hospitals and products may be reimbursed by the Social Security Fund. The price of medicines is negotiated with the Economic Committee for Health Products. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our product candidates. Historically, products launched in the European Union do not follow price structures of the United States and generally prices in the European Union tend to be significantly lower than prices in the United States

***Enacted and future healthcare legislation may increase the difficulty and cost for us to progress our clinical programs and obtain marketing approval of and commercialize our product candidates and may affect the prices we may set.***

In the United States and other jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes and proposed changes to the healthcare system that could affect our future results of operations. 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. Individual states in the United States have also 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. See the section entitled “*Business — Healthcare Reform*” included above in this filing.

We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the extent to which state and federal governments cover particular healthcare products and services and could limit the amounts that the federal and state governments will pay for healthcare products and services. This could result in reduced demand for any product candidate we develop or could result in additional pricing pressures.

In markets outside of the United States, reimbursement and healthcare payment systems vary significantly by country and many countries have instituted price ceilings on specific products and therapies. The price control regulations outside of the United States can have a significant impact on the profitability of a given market, and further uncertainty is introduced if and when these laws change.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action in the United States or any other jurisdiction. It is possible that additional governmental action will be taken in response to the ongoing COVID-19 pandemic. If we or any third parties we may engage are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we or these third parties are not able to maintain regulatory compliance, our product candidates may lose any regulatory approval that may have been obtained and we may not achieve or sustain profitability.

***We may face potential liability under applicable privacy laws if we obtain identifiable patient health information from clinical trials sponsored by us.***

Most healthcare providers, including certain research institutions from which we may obtain patient health information, are subject to privacy and security regulations promulgated under the Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act. Depending on the facts and circumstances, we could be subject to civil, criminal, and administrative penalties if we obtain, use, or disclose individually identifiable health information maintained by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA. In addition, we may be subject to state laws requiring notification of affected

individuals and state regulators in the event of a breach of personal information, which is a broader class of information than the health information protected by HIPAA.

The global data protection landscape is rapidly evolving, and we may be or become subject to or affected by numerous federal, state, and foreign laws and regulations, as well as regulatory guidance, governing the collection, use, disclosure, transfer, security and processing of personal data, such as information that we collect about participants and healthcare providers in connection with clinical trials. Implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future, which may create uncertainty in our business, affect our or our service providers' ability to operate in certain jurisdictions or to collect, store, transfer use and share personal data, result in liability or impose additional compliance or other costs on us. Any failure or perceived failure by us to comply with federal, state or foreign laws or self-regulatory standards could result in negative publicity, diversion of management time and effort, and proceedings against us by governmental entities or others.

In the United States, the California Consumer Privacy Act of 2018, or the CCPA, went into effect in January 2020. The CCPA provides new data privacy rights for consumers and new operational requirements for companies, including placing increased privacy and security obligations on entities handling certain personal data of consumers or households. These requirements could increase our compliance costs and potential liability. The CCPA gives California residents expanded rights to access and delete their personal information, opt out of certain personal information sharing and receive detailed information about how their personal information is used. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. While there is currently an exception for protected health information that is subject to HIPAA and clinical trial regulations, as currently written, the CCPA may impact certain of our business activities. Additionally, a new California ballot initiative, the California Privacy Rights Act, or CPRA, was passed in November 2020. The CPRA, which became effective on January 1, 2023 imposes additional obligations on companies covered by the legislation and significantly modifies the CCPA, including by expanding consumers' rights with respect to certain sensitive personal information. The CPRA also creates a new state agency that will be vested with authority to implement and enforce the CCPA and the CPRA. The effects of the CCPA and the CPRA are potentially significant and may require us to modify our data collection or processing practices and policies and to incur substantial costs and expenses in an effort to comply and increase our potential exposure to regulatory enforcement and/or litigation.

Also, on March 2, 2021, Virginia enacted the Consumer Data Protection Act, or CDPA, which became effective January 1, 2023. In addition, on July 8, 2021, Colorado's governor signed the Colorado Privacy Act, or CPA, into law and on March 24, 2022, Utah's governor signed into law the Utah Consumer Privacy Act (UCPA) which will take effect on December 31, 2023. Finally, in May 2022, Connecticut Governor Lamont signed the Connecticut Data Privacy Act, or CTDPA, into laws. The UCPA and CTDPA draw heavily upon their predecessors in Virginia and Colorado.

With the CTDPA, Connecticut became the fifth state to enact a comprehensive privacy law, but it is quite possible that other states will follow suit and bills have been proposed in many states. Such proposed legislation, if enacted, may add additional complexity, further variation in requirements, restrictions, and potential legal risk, require additional investment of resources in compliance programs, impact strategies and the availability of previously useful data and could result in increased compliance costs and/or changes in business practices and policies. The existence of comprehensive privacy laws in different states in the country will make our compliance obligations more complex and costly and may increase the likelihood that we may be subject to enforcement actions or otherwise incur liability for noncompliance.

***The increasing number and complexity of privacy and data protection laws, and other changes in laws or regulations across the globe, especially those associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could lead to government enforcement actions and significant penalties against us and could have a material adverse effect on our business, financial condition, or results of operations.***

Outside of the United States, we also face the challenge of stringent privacy and data protection laws. For example, legislators in the European Economic Area, or the EEA, adopted the EU General Data Protection Regulation, or GDPR, which became effective on May 25, 2018 and the EU GDPR and, as transposed into the laws of the UK, the UK GDPR, collectively referred to as the GDPR. The GDPR imposes more stringent data protection compliance requirements on controllers and processors of personal data, including special protections for "special category data," which includes health, biometric, and genetic information of data subjects located in the EEA and UK and provides for more significant penalties for noncompliance. Further, the GDPR provides a broad right for EEA Member States to create supplemental national laws, such as laws relating to the processing of health, genetic, and biometric data, which could further limit our ability to use and share such data or could cause our costs to increase, and harm our business and financial condition. The GDPR creates new compliance obligations that may be applicable to our business, which could cause us to change our business practices, and increases financial penalties for noncompliance (including possible fines of up to the greater of €20 million (£17.5 million under the UK GDPR) and 4% of our global annual turnover for the preceding financial year for the most



serious violations, as well as the right to compensation for financial or non-financial damages claimed by any individuals under Article 82 of the GDPR). In addition to such fines, we may be the subject of litigation and/or adverse publicity, which could have a material adverse effect on our reputation and business.

The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR includes restrictions on cross-border data transfers. The GDPR may increase our responsibility and liability in relation to personal data that we process where that processing is subject to the GDPR. In addition, we may be required to put in place additional mechanisms to ensure compliance with the GDPR, including GDPR requirements as implemented by individual countries.

As a result of the implementation of the GDPR, we are required to put in place a number of measures to ensure compliance with the data protection regime. The GDPR requires us to inform data subjects of how we process their personal data and how they can exercise their rights, ensure we have a valid legal basis to process personal data (if this is consent, the requirements for obtaining consent carries a higher threshold), and appoint a data protection officer where sensitive personal data (i.e., health data) is processed on a large scale. In addition, the GDPR introduces mandatory data breach notification requirements throughout the EEA and UK, requires us to maintain records of our processing activities and to document data protection impact assessments where there is high risk processing, imposes additional obligations on us when we are contracting with service providers, requires appropriate technical and organizational measures be put in place to safeguard personal data and requires us to adopt appropriate privacy governance including policies, procedures, training and data audit. We are taking steps to comply with the GDPR as appropriate and as and when applicable to us, but this is an ongoing compliance process. Compliance with the GDPR will be a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices. If our efforts to comply with GDPR or other applicable EU and UK laws and regulations are not successful, or are perceived to be unsuccessful, it could adversely affect our business in the EU and/or the UK.

Significantly, the GDPR imposes strict rules on the transfer of personal data out of the EEA and UK to the United States or other regions that have not been deemed to offer “adequate” privacy protections. In the past, companies in the United States were able to rely upon the EU-United States, UK-United States, and the Swiss-United States Privacy Shield frameworks to legitimize data transfers from the EU and the UK to the United States. In July 2020, the Court of Justice of the European Union, or CJEU, in Case C-311/18 (Data Protection Commissioner v Facebook Ireland and Maximilian Schrems, or Schrems II) invalidated the EU-United States Privacy Shield on the grounds that the Privacy Shield failed to offer adequate protections to EU personal data transferred to the United States. The CJEU, in the same decision, deemed that the Standard Contractual Clauses, or SCCs, published by the European Commission, or the EC, are valid. However, the CJEU ruled that transfers made pursuant to the SCCs need to be assessed on a case-by-case basis to ensure the law in the recipient country provides “essentially equivalent” protections to safeguard the transferred personal data as the EU, and required businesses to adopt supplementary measures if this standard is not met. Subsequent guidance published by the European Data Protection Board in June 2021 described what these supplementary measures must be, and stated that businesses should avoid or cease transfers of personal data if, in the absence of supplementary measures, equivalent protections cannot be afforded. On June 4, 2021, the EC published new versions of the SCCs, which seek to address the issues identified by the CJEU’s Schrems II decision and provide further details regarding the transfer assessments that the parties are required to conduct when implementing the new SCCs. However, there continue to be concerns about whether the SCCs and other mechanisms will face additional challenges. Similarly, the Swiss data protection authority determined the Swiss-United States Privacy Shield framework was no longer a valid mechanism for Swiss-United States data transfers and also raised questions about the validity of the SCCs as a mechanism for transferring personal data from Switzerland. While the SCCs provide an alternative to the Privacy Shield certification for EU-United States data flows, the decision (and certain regulatory guidance issued in its wake) casts doubt on the legality of EU-United States data flows in general. Any inability to transfer personal data from the EU to the United States in compliance with data protection laws may impede our ability to conduct trials and may adversely affect our business and financial position. The UK is not subject to the EC’s new SCCs but has published its own transfer mechanism, the International Data Transfer Agreement or International Data Transfer Addendum, which enables transfers from the UK. On March 25, 2022, the EC and the US announced that they have reached a political agreement on a new “Trans-Atlantic Data Privacy Framework,” which will replace the invalidated Privacy Shield and, on December 13, 2022, the EC published a draft adequacy decision on the Trans-Atlantic Data Privacy Framework.

In addition, EEA Member States have adopted national laws to implement the GDPR that may partially deviate from the GDPR. Further, the competent authorities in the EEA Member States may interpret GDPR obligations slightly differently from country to country and therefore we do not expect to operate in a uniform legal landscape in the EEA.

Outside of the United States and Europe, many jurisdictions in which we have CROs or otherwise do business are also considering and/or have enacted comprehensive data protection legislation. In addition, the UK has announced plans to reform the country’s data protection legal framework in its Data Reform Bill, but these have been put on hold. We may,

however, incur liabilities, expenses, costs, and other operational losses under the GDPR and applicable EEA Member States and the UK privacy laws in connection with any measures we take to comply with them.

We are subject to the supervision of local data protection authorities in those jurisdictions where we are monitoring the behavior of individuals in the EEA or UK (i.e., undertaking clinical trials). We depend on a number of third parties in relation to the provision of our services, a number of which process personal data of EEA and/or UK individuals on our behalf. With each such provider we enter or intend to enter into contractual arrangements under which they are contractually obligated to only process personal data according to our instructions, and conduct or intend to conduct diligence to ensure that they have sufficient technical and organizational security measures in place.

Further, certain health privacy laws, data breach notification laws, consumer protection laws and genetic testing laws may apply directly to our operations and/or those of our collaborators and may impose restrictions on our collection, use and dissemination of individuals' health information. Patients about whom we or our collaborators may obtain health information, as well as the providers who may share this information with us, may have statutory or contractual rights that limit our ability to use and disclose the information. We may be required to expend significant capital and other resources to ensure ongoing compliance with applicable privacy and data security laws. Claims that we have violated individuals' privacy rights or breached our contractual obligations, even if we are not found liable, could be expensive and time-consuming to defend and could result in adverse publicity that could harm our business.

If we or third-party CMOs, CROs or other contractors or consultants fail to comply with applicable federal, state/provincial or local regulatory requirements, we could be subject to a range of regulatory actions that could affect our or our contractors' ability to develop and commercialize our therapeutic candidates and could harm or prevent sales of any affected therapeutics that we are able to commercialize, or could substantially increase the costs and expenses of developing, commercializing, and marketing our therapeutics. Any threatened or actual government enforcement action could also generate adverse publicity and require that we devote substantial resources that could otherwise be used in other aspects of our business. Increasing use of social media could give rise to liability, breaches of data security or reputational damage.

Additionally, we are subject to state and foreign equivalents of each of the healthcare laws described above, among others, some of which may be broader in scope and may apply regardless of the payor.

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

We are subject to numerous environmental, health, and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment, and disposal of hazardous materials and wastes. Our research and development activities involve the use of biological and hazardous materials and produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials, which could cause an interruption of our commercialization efforts, research and development efforts and business operations, environmental damage resulting in costly clean-up and liabilities under applicable laws and regulations governing the use, storage, handling, and disposal of these materials and specified waste products. Although we believe that the safety procedures utilized by our third-party CMOs for handling and disposing of these materials generally comply with the standards prescribed by these laws and regulations, we cannot guarantee that this is the case or eliminate the risk of accidental contamination or injury from these materials. Upon an event of this nature, we may be held liable for any resulting damages and such liability could exceed our resources and state or federal or other applicable authorities may curtail our use of certain materials and/or interrupt our business operations. Further, environmental laws and regulations are complex, change frequently, and have tended to become more stringent. We cannot predict the impact of any changes of this nature and cannot be certain of our future compliance. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development, or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties, or other sanctions.

Although we maintain workers' compensation insurance to cover us for costs and expenses, we may incur due to injuries to our employees resulting from the use of hazardous materials or other work-related injuries, this insurance may not provide adequate coverage against potential liabilities. We do not carry specific biological waste or hazardous waste insurance coverage, workers compensation or property and casualty and general liability insurance policies that include coverage for damages and fines arising from biological or hazardous waste exposure or contamination.

***We are subject to United States and certain foreign export and import controls, sanctions, embargoes, anti-corruption laws, and anti-money laundering laws and regulations. Compliance with these legal standards could impair our ability***

*to compete in domestic and international markets. We can face criminal liability and other serious consequences for violations, which can harm our business.*

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls, the U.S. Foreign Corrupt Practices Act of 1977, as amended, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act of 2001 and other state and national anti-bribery and anti-money laundering laws in the countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, contractors, and other collaborators from authorizing, promising, offering or providing, directly or indirectly, improper payments or anything else of value to recipients in the public or private sector. In the future, 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 may also have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. We can be held liable for the corrupt or other illegal activities of our employees, agents, contractors, and other collaborators, even if we do not explicitly authorize or have actual knowledge of these activities. Any violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences.

**Risks related to employee matters, managing growth, and operational matters**

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

Our ability to compete in the highly competitive biotechnology and pharmaceutical industries depends upon our ability to attract and retain highly qualified managerial, scientific, medical personnel, sales and marketing, and other personnel. We are highly dependent on our management, scientific and medical personnel, including our President and Chief Executive Officer, Chief Scientific Officer, Chief Medical Officer, Chief Financial Officer, Chief Legal Officer, Chief People Officer, and Chief Business Officer. Our Chief Medical Officer resigned in February 2023 and we have engaged an interim Chief Medical Officer while we complete a search for a permanent Chief Medical Officer. While we expect to engage in an orderly transition process if and when we integrate newly appointed officers and managers, we face a variety of risks and uncertainties relating to management transition, including diversion of management attention from business concerns, failure to retain other key personnel, or loss of institutional knowledge. In addition, the loss of the services of any of our executive officers, other key employees, and other scientific and medical advisors, and an inability to find suitable replacements could result in delays in product development, and harm our business.

We conduct our operations at our facilities in Watertown, Massachusetts. The Massachusetts region is headquarters to many other biopharmaceutical companies and many academic and research institutions. Competition for skilled personnel in our market is intense and may limit our ability to hire and retain highly qualified personnel on acceptable terms or at all. Changes to U.S. immigration and work authorization laws and regulations, including those that restrain the flow of scientific and professional talent, can be significantly affected by political forces and levels of economic activity. Our business may be materially adversely affected if legislative or administrative changes to immigration or visa laws and regulations impair our hiring processes and goals or projects involving personnel who are not U.S. citizens.

To encourage valuable employees to remain at our company, in addition to salary and cash incentives, we have provided stock options and other equity awards that vest over time or based on the achievement of milestones. The value to our employees of equity awards that vest over time may be significantly affected by movements in our stock price that are beyond our control and may, at any time, be insufficient to counteract more lucrative offers from other companies. The same may be true in respect of equity awards that vest based on the achievement of milestones. Despite our efforts to retain valuable employees, members of our management, scientific and development teams may terminate their employment with us on short notice. Although we have employment agreements with our executive employees, these employment agreements provide for at-will employment, which means that any of our executive employees could leave our employment at any time, with or without notice. Our success also depends on our ability to continue to attract, retain and motivate highly skilled junior, mid-level, and senior managers, as well as junior, mid-level, and senior scientific, medical, and general and administrative personnel.

In addition, we have scientific and clinical advisors who assist us in formulating our development and clinical strategies. These advisors are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us. In addition, our advisors may have arrangements with other companies to assist those companies in developing products or technologies that may compete with ours.

***We will need to grow the size of our organization and we may experience difficulties in managing this growth, which could disrupt our operations.***

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, manufacturing, regulatory affairs and, if any of our product candidates receives or is expected to receive marketing approval, sales, marketing, and distribution. In the future, we may need to increase the size of our general and administrative teams to support the growth of our business, our stage of company and/or the requirements of being a publicly traded company. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational, and financial systems, expand our facilities, and continue to recruit and train additional qualified personnel. Future growth would impose significant added responsibilities on members of management, including:

- identifying, recruiting, integrating, maintaining, and motivating additional employees;
- managing our internal development efforts effectively, including the clinical and FDA review process for our lead product candidates and any other product candidates we develop, while complying with our contractual obligations to contractors and other third parties; and
- improving our operational, financial and management controls, reporting systems, and procedures.

Our future financial performance and our ability to advance into clinical development and, if approved, commercialize our lead product candidates and any of our other product candidates we develop will depend, in part, on our ability to effectively manage any future growth. Due to our limited financial resources and the limited experience of our management team in managing a company with this type of anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations. Further, research at our Chinese and Indian CROs also exposes us to various risks, including regulatory, economic, and political instability, potentially unfavorable tax, import and export policies, fluctuations in foreign exchange and inflation rates, international and civil hostilities, terrorism, natural disasters, and pandemics.

***Our internal computer systems, or those of any of our collaborators, vendors, contractors, or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs and could harm our reputation or subject us to liability, and adversely affect our business and financial results.***

Our internal computer systems and those of any collaborators, vendors, contractors or consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war, and telecommunication and electrical failures. While we have not experienced any material system failure, accidents, or security breaches of this nature to date, if an event of this nature were to occur and cause interruptions in our operations, 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 proprietary information or other similar disruptions. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our marketing approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of or damage to our data or applications or the inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position could be harmed, and the further development and commercialization of our product candidates could be delayed. Additionally, we may have data security obligations with respect to the information of third parties that we store. Unauthorized access or use of any third-party data or information of this nature could result in fines or other penalties that may impact our relationships with these third parties and our operations.

Any actual or perceived security breach of our platform, systems, and networks could damage our reputation and brand, expose us to a risk of litigation and possible liability, and require us to expend significant capital and other resources to respond to and alleviate problems caused by the security breach. Our ability to maintain adequate cyber-crime and liability insurance may be reduced. Some jurisdictions have enacted laws requiring companies to notify individuals of data security breaches involving certain types of personal data and our agreements with certain partners require us to notify them in the event of a security incident. These types of mandatory disclosures are costly, could lead to negative publicity, and may cause our partners to lose confidence in the effectiveness of our data security measures. Any of these events could harm our reputation or subject us to liability, and materially and adversely affect our business and financial results. Although we maintain cyber liability insurance, we cannot be certain that its coverage will be adequate for liabilities actually incurred or that insurance will continue to be available to us on economically reasonable terms, or at all.

***Our employees, independent contractors, vendors, principal investigators, CROs, and consultants may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements, and insider trading laws.***

We are exposed to the risk that our employees, independent contractors, vendors, principal investigators, CROs, CMOs, and consultants may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include, among other things:

- intentional, reckless, or negligent conduct or disclosure of unauthorized activities that violate study and trial protocols or the regulations of the FDA or similar foreign regulatory authorities;
- violations of healthcare fraud and abuse laws and regulations in the United States and abroad;
- violations of U.S. federal securities laws relating to trading in our common stock; and
- failures to report financial information or data accurately.

In particular, sales, marketing, and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing, and other abusive practices. These laws and regulations regulate a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs, and other business arrangements. Other forms of misconduct could involve the improper use of information obtained in the course of clinical trials or creating fraudulent data in our preclinical studies or clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of business conduct and ethics and other corporate governance and compliance documents, policies and charters applicable to all of our employees. However, it is not always possible to identify and deter misconduct by employees and other third parties. Further, the precautions we take to detect and prevent this type of activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. Additionally, we are subject to the risk that a person could allege fraud or other misconduct, even if none occurred. If any actions of this nature are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and/or curtailment of our operations, any of which could adversely affect our business prospects, financial condition, and results of operations.

#### **Risks related to our common stock**

***If we were to determine to raise additional capital in the future, you would suffer dilution of your investment.***

We may choose to raise additional capital in the future through the sale of shares or other securities convertible into shares, depending on market conditions, strategic considerations, and operational requirements. To the extent we raise additional capital in this manner, our stockholders will be diluted. Future issuances of our common stock or other equity securities, or the perception that sales of this nature may occur, could adversely affect the trading price of our common stock, and impair our ability to raise capital through future offerings of shares or equity securities. No prediction can be made as to the effect, if any, that future sales of common stock or the availability of common stock for future sales will have on the trading price of our common stock.

***We do not know whether an active, liquid, and orderly trading market will be sustained for our common stock or what the market price of our common stock will be and, as a result, it may be difficult for you to sell your shares of our common stock.***

Prior to our initial public offering, there was no public trading market for shares of our common stock. Although our common stock is listed on The Nasdaq Global Select Market, an active trading market for our shares may not be sustained. You may not be able to sell your shares quickly or at the market price if trading in shares of our common stock is not active. Further, an inactive market may also impair our ability to raise capital by selling shares of our common stock and may impair our ability to enter into strategic partnerships or acquire companies or products by using our shares of common stock as consideration.

***If securities or industry analysts do not publish or cease publishing research or reports about our business, or if they issue an adverse or misleading opinion regarding our stock, our stock price, and trading volume could decline.***

The trading market for our common stock is and will continue to be influenced by the research and reports that industry or securities analysts publish about us, our business or the targeted protein degradation space. We do not have control over these analysts. There can be no assurance that existing analysts will continue to provide research coverage or that new analysts will begin to provide coverage. Although we have obtained analyst coverage, if any of the analysts who cover us

were to issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our preclinical studies and future clinical trials and results of operations fail to meet the expectations of any of these analysts, our stock price would likely decline. If one or more of these covering analysts were to cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause a decline in our stock price or trading volume.

***The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for purchasers of our common stock.***

The trading price of shares of our common stock has been and may continue to be volatile and subject to wide fluctuations in response to various factors, some of which we cannot control. The stock market in general, and the market for smaller biopharmaceutical companies in particular, have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your common stock at or above the price at which you acquired it. The market price for our common stock may be influenced by many factors, including:

- the degree of success of competitive products or technologies or changes in standard of care regimens;
- results of preclinical studies and clinical trials of our product candidates or those of our competitors;
- the timing and progress of our clinical development activities;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs and the value of the cash, cash equivalents, and marketable securities we hold;
- the results of our efforts to discover, develop, acquire or in-license additional technologies or product candidates;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- effects of public health crises, pandemics and epidemics, such as COVID-19;
- general economic, industry, and market conditions; and
- the other factors described in this “Risk Factors” section.

If any of the foregoing factors were viewed as likely to have a negative impact on our business, prospects or operations or if our operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. In the past, following periods of volatility in the market price of a company’s securities, securities class-action litigation often has been instituted against that company. Litigation of this nature, if instituted against us, could cause us to incur substantial costs to defend these claims and divert management’s attention and resources, which could seriously harm our business, financial condition, results of operations, and prospects. Further, our director and officer liability insurance cost may increase as a result of litigation of this nature and our insurance deductible may be significant before our insurers are required to provide any coverage to us.

***We have broad discretion in the use of the capital we have raised and may not use our capital effectively.***

Our management has broad discretion in the application of the net proceeds from our prior financings, including our initial and follow-on public offerings, and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have an adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we may invest the net proceeds from our financing activities in a manner that does not produce income or that loses value.

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

Our executive officers and directors, combined with our stockholders who have reported through filings made with the Securities and Exchange Commission that they own more than 5% of our outstanding common stock, in the aggregate, beneficially own a significant percentage of our shares. As a result, our executive officers and directors, combined with our greater than 5% stockholders, have the ability to control us through this ownership position. These stockholders, if acting together, will consequently continue to control matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would control the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of ownership control may:

- delay, defer or prevent a change in control;
- entrench our management and the board of directors; or
- impede a merger, consolidation, takeover or other business combination involving us that other stockholders may desire.

***Anti-takeover provisions under our charter documents and Delaware law could delay or prevent a change of control, which could limit the market price of our common stock and may prevent or frustrate attempts by our stockholders to replace or remove our current management.***

Our amended and restated certificate of incorporation and amended and restated by-laws contain provisions that could delay or prevent a change of control of our company or changes in our board of directors that our stockholders might consider favorable. Some of these provisions include:

- a board of directors divided into three classes serving staggered three-year terms, the result of which is that not all members of the board will be elected at one time;
- a prohibition on stockholder action through written consent, the result of which is that all stockholder actions will have to be taken at a meeting of our stockholders;
- a requirement that special meetings of stockholders be called only by the board of directors acting pursuant to a resolution approved by the affirmative vote of a majority of the directors then in office;
- advance notice requirements for stockholder proposals and nominations for election to our board of directors;
- a requirement that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of not less than two-thirds of all outstanding shares of our voting stock then entitled to vote in the election of directors;
- a requirement of approval of not less than two-thirds of all outstanding shares of our voting stock to amend any by-laws by stockholder action or to amend specific provisions of our certificate of incorporation; and
- the authority of the board of directors to issue preferred stock on terms determined by the board of directors without stockholder approval and which preferred stock may include rights superior to the rights of the holders of common stock.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporate Law, which may prohibit certain business combinations with stockholders owning 15% or more of our outstanding voting stock. These anti-takeover provisions and other provisions in our amended and restated certificate of incorporation and amended and restated by-laws could make it more difficult for stockholders or potential acquirers to obtain control of our board of directors or initiate actions that are opposed by the then-current board of directors and could also delay or impede a merger, tender offer, or proxy contest involving our company. These provisions could also discourage proxy contests and make it more difficult for you and other stockholders to elect directors of your choosing or cause us to take other corporate actions you desire. Any delay or prevention of a change of control transaction or changes in our board of directors could cause the market price of our common stock to decline.

***We will continue to incur additional costs as a result of operating as a public company and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices.***

As a public company, we will continue to incur significant legal, accounting, and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, or Sarbanes-Oxley, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The Nasdaq Stock Market LLC and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective

disclosure and financial controls and corporate governance practices. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations increase our legal and financial compliance and insurance costs and make some activities more time-consuming and costly. For example, these rules and regulations make it more difficult and more expensive for us to obtain director and officer liability insurance, which in turn could make it more difficult for us to attract and retain qualified members of our board of directors.

We continually evaluate these rules and regulations and cannot always predict or estimate the amount of additional costs we may incur or the timing of these costs. These rules and regulations are also often subject to varying interpretations, in many cases due to their lack of specificity and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404 of Sarbanes-Oxley, or Section 404, we are required to furnish a report by our management on our internal control over financial reporting. However, as a “smaller reporting company,” we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm until we are no longer a smaller reporting company. As of the end of our fiscal year ended December 31, 2022, we qualified as a “non-accelerated filer” as defined in the Securities Exchange Act of 1934, as amended, or the Exchange Act and as a “smaller reporting company.” Our compliance with Section 404 necessitates that we incur substantial accounting expense and expend significant management efforts.

We will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk we will be unable to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. Further, we cannot assure you that the measures we have taken in the past or will take in the future will prevent the occurrence of future material weaknesses or significant deficiencies in our internal control over financial reporting. If we identify one or more material weaknesses in the future, it could result in an adverse reaction in the financial markets and restrict our future access to the capital markets due to a loss of confidence in the reliability of our consolidated financial statements.

***Our amended and restated by-laws designate specific courts as the exclusive forum for certain litigation that may be initiated by our stockholders, which could limit our stockholders’ ability to obtain a favorable judicial forum for disputes with us.***

Pursuant to our amended and restated by-laws, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware is the sole and exclusive forum for state law claims for (i) any derivative action or proceeding brought on our behalf; (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, or other employees to us or our stockholders; (iii) any action asserting a claim arising pursuant to any provision of the Delaware General Corporation Law or our amended and restated certificate of incorporation or amended and restated by-laws; (iv) any action to interpret, apply, enforce or determine the validity of our amended and restated certificate of incorporation or amended and restated by-laws; or (v) any action asserting a claim governed by the internal affairs doctrine. We refer to this provision in our amended and restated by-laws as the Delaware Forum Provision. The Delaware Forum Provision will not apply to any causes of action arising under the Securities Act of 1933, as amended, the Securities Act, or the Exchange Act of 1934, as amended, or the Exchange Act.

Our amended and restated by-laws further provide that unless we consent in writing to the selection of an alternative forum, the U.S. District Court for the District of Massachusetts shall be the sole and exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act, as our headquarters are located in Watertown, Massachusetts. We refer to this provision in our amended and restated by-laws as the Federal Forum Provision. In addition, our amended and restated by-laws provide that any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock is deemed to have notice of and consented to the Delaware Forum Provision and the Federal Forum Provision.

The Delaware Forum Provision and the Federal Forum Provision in our amended and restated by-laws may impose additional litigation costs on stockholders in pursuing any such claims. Additionally, these forum selection clauses may limit our stockholders’ ability to bring a claim in a judicial forum that they find favorable for disputes with us or our directors, officers or employees, and may discourage the filing of lawsuits against us and our directors, officers, and employees, even though an action, if successful, might benefit our stockholders. In addition, while the Delaware Supreme Court ruled in March 2020 that federal forum selection provisions purporting to require claims under the Securities Act be brought in federal court are “facially valid” under Delaware law, there is uncertainty as to whether other courts will enforce our Federal Forum Provision. If the Federal Forum Provision is found to be unenforceable, we may incur additional costs associated with resolving such matters. The Federal Forum Provision may also impose additional litigation costs on



stockholders who assert that the provision is not enforceable or invalid. The Court of Chancery of the State of Delaware and the U.S. District Court for the District of Massachusetts may also reach different judgments or results than would other courts, including courts where a stockholder considering an action may be located or would otherwise choose to bring the action, and such judgments may be more or less favorable to us than our stockholders.

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

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of our Credit Agreement with Perceptive Credit also preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

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

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. For example, the global financial crisis caused extreme volatility and disruptions in the capital and credit markets. Similarly, the recent significant volatility associated with the ongoing COVID-19 pandemic has caused significant instability and disruptions in the capital and credit markets. In recent months, we have observed increased economic uncertainty in the United States and abroad. Our operations could be adversely affected by economic and political changes in the markets, including higher inflation rates, supply chain disruptions, recessions, trade restrictions, tariff increases or potential new tariffs, and economic embargoes imposed by the United States. A severe or prolonged economic downturn could result in a variety of risks to our business, including weakened demand for our product candidates, and could also impact our ability to raise additional capital when needed on acceptable terms, if at all. Our general business strategy may be adversely affected by any economic downturn of this nature, volatile business environment or continued unpredictable and unstable market conditions. If the current equity and credit markets deteriorate, or do not improve, it may make any necessary debt or equity financing more difficult, costly and dilutive, or not available at all.

Failure to secure any necessary financing in a timely manner and on favorable terms could have an adverse effect on our growth strategy, financial performance, and stock price, and could require us to delay, modify, 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 these difficult economic times, which could directly affect our ability to attain our operating goals on schedule and on budget.

The outstanding debt under our term loan with Perceptive Credit Holdings III, LP bears interest at a variable rate using the greater of LIBOR or 1.75%, plus 9.50%. The loan is secured by a lien on substantially all of our assets. Continued increases in interest rates could increase the cost of servicing or refinancing our outstanding indebtedness, and could adversely affect our results of operations, financial condition, liquidity, and cash flows.

Historically, 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 pharmaceutical companies have experienced significant stock price volatility in recent years. If we were to be sued, it could result in substantial costs and a diversion of management's attention and resources, which could adversely affect our business prospects, financial condition, and results of operations.

**Item 1B. Unresolved Staff Comments.**

Not applicable.

**Item 2. Properties.**

We currently lease approximately 111,611 square feet of office and laboratory space in Watertown, Massachusetts under a lease that expires in 2032. In June 2022, we entered into a sublease agreement for approximately 30,067 square feet of our office and laboratory space in Watertown, Massachusetts, which expires in 2025. We believe that our facilities are sufficient to meet our current needs for the foreseeable future and that suitable additional space will be available as and when needed.

**Item 3. Legal Proceedings.**

We are not currently a party to any material legal proceedings. From time to time, we may be subject to various legal proceedings and claims that arise in the ordinary course of our business activities. Regardless of the outcome, litigation can have a material adverse effect on us because of defense and settlement costs, diversion of management resources, and other factors.

**Item 4. Mine Safety Disclosures.**

Not applicable.

## PART II

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

#### **Market information**

Our common stock has been publicly traded on the Nasdaq Global Select Market under the symbol “CCCC” since October 2, 2020. Prior to that time, there was no public market for our common stock.

#### **Holders**

As of February 15, 2023, there were approximately 60 holders of record of our common stock. This number does not include beneficial owners whose shares are held by nominees in street name.

#### **Dividends**

We have not declared or paid any cash dividends on our capital stock since our inception. We intend to retain future earnings, if any, to finance the operation and expansion of our business and do not anticipate paying any cash dividends to holders of common stock in the foreseeable future.

#### **Securities authorized for issuance under equity compensation plans**

Information about our equity compensation plans is incorporated herein by reference to Item 12, *Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters*, of this Annual Report on Form 10-K.

#### **Recent sales of unregistered securities**

None.

#### **Use of proceeds from registered securities**

In October 2020, our Registration Statement on Form S-1 (No. 333-248719) was declared effective by the SEC pursuant to which we issued and sold an aggregate of 11,040,000 shares of common stock, including 1,440,000 shares sold pursuant to the underwriters’ exercise of their over-allotment option, at a public offering price of \$19.00 per share for aggregate net cash proceeds of \$191.2 million, after deducting underwriting discounts, commissions, and offering costs. No payments for such expenses were made directly or indirectly to (i) any of our officers or directors or their associates, (ii) any persons owning 10% or more of any class of our equity securities or (iii) any of our affiliates. The sale and issuance of 11,040,000 shares closed on October 6, 2020. Jefferies LLC, Evercore Group L.L.C., BMO Capital Markets Corp., and UBS Securities LLC acted as joint book-running managers for the offering. Upon commencement, the offering did not terminate until the sale of all the shares offered.

Our use of the net offering proceeds through the date of the filing of this Annual Report on Form 10-K, is consistent with the use of proceeds described in our prospectus filed with the SEC pursuant to Rule 424(b)(4) in October 2020, and there has been no material change in our planned use of the balance of the net proceeds from the offering described in the prospectus.

#### **Purchases of equity securities by the issuer or affiliated purchasers**

Neither we nor any affiliated purchaser or anyone acting on our behalf or on behalf of an affiliated purchaser made any purchases of shares of our common stock during the year ended December 31, 2022.

#### **Item 6. [Reserved]**

Not applicable.

### **Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations.**

*The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our consolidated financial statements and the related notes to those statements included elsewhere in this Annual Report on Form 10-K. In addition to historical financial information, the following discussion and analysis contains forward-looking statements that involve risks, uncertainties, and assumptions. Some of the numbers included herein have been rounded for the convenience of presentation. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of many factors, including those discussed under Item 1A, Risk factors, in this Annual Report on Form 10-K.*

## Overview

We are a clinical-stage biopharmaceutical company dedicated to advancing targeted protein degradation science to develop a new generation of small-molecule medicines to transform how disease is treated. Historically, the focus in our industry has been on discovering and developing small molecule medicines that inhibit the activity of disease-causing proteins. However, that approach has been limited to only those proteins where chemistry can be used to bind to active sites on the protein and effectively inhibit its activity, which accounts for less than 15% of the human proteome. Furthermore, for those targets where inhibitors have been approved, resistance mechanisms emerge that ultimately render inhibitor approaches ineffective over time. We leverage our proprietary technology platform, which we call TORPEDO, to efficiently design and optimize small-molecule medicines that harness the body's natural protein recycling system to rapidly degrade disease-causing protein, offering the potential to overcome resistance mechanisms, target the 85% of the human proteome deemed undruggable, and improve patient outcomes. We are using our TORPEDO platform to advance multiple targeted oncology programs to the clinic while expanding the platform to deliver the next wave of medicines for difficult-to-treat diseases and ultimately improve treatment options for patients.

Our most advanced product candidate, CFT7455, is an orally bioavailable MonoDAC degrader of protein targets called IKZF1 and IKZF3, currently in clinical development for MM, and NHLs. We have selected IKZF1 and IKZF3 as our initial targets because they have a strong mechanistic rationale, a well-defined biology, and targeting them with a novel degrader may address a significant unmet need. In our preclinical studies, CFT7455 has demonstrated potent and selective protein degradation with favorable pharmacological properties. We initiated a first-in-human Phase 1/2 clinical trial for this product candidate in June 2021. In August 2021, the FDA, granted orphan drug designation to CFT7455 for the treatment of MM. We presented initial clinical data from Arm A at the American Association for Cancer Research Annual Meeting in April 2022. These data showed that single agent CFT7455 resulted in deep and durable degradation of IKZF1/3, as quantified by mass spectrometry, and meaningful decreases in serum free light chain. Neutropenia, a known on-target toxicity associated with IKZF1/3 degraders, was dose-limiting at the 50 µg starting dose on a dosing schedule with a seven-day drug holiday over a 28-day cycle. As a result, the dosing schedule was modified to include a 14-day drug holiday over a 28-day cycle. We continue to enroll patients in the Phase 1 dose escalation portion of the ongoing Phase 1/2 clinical trial at the modified schedule.

Our next most advanced product candidate, CFT8634, is an orally bioavailable BiDAC degrader of a protein target called BRD9, currently in clinical development for synovial sarcoma and SMARCB1-null solid tumors. Historically, BRD9 has been considered an “undruggable” target due to the inability of bromodomain inhibitors to effectively treat cancers dependent on BRD9. Unlike BRD9 inhibition, BRD9 degradation has been shown to be efficacious in preclinical models of synovial sarcoma. In preclinical studies, CFT8634 has shown potent anti-tumor activity in synovial sarcoma cell lines but does not appear to affect normal cells. Further, CFT8634 has shown *in vivo* activity in synovial sarcoma xenograft models when dosed orally. In March 2022, the FDA granted orphan drug designation to CFT8634 for the treatment of soft tissue sarcoma. In May 2022, we initiated the first-in-human Phase 1/2 clinical trial of this product candidate. In January 2023, we shared initial PK and PD data from the initial dose escalation cohorts of the Phase 1/2 trial that demonstrate dose proportional exposure, strong oral bioavailability and deep BRD9 degradation. We continue to enroll patients in the Phase 1 dose escalation portion of the ongoing clinical trial.

We are also developing CFT1946, an orally bioavailable BiDAC degrader specifically to be potent and selective against BRAF V600 mutant targets to treat melanoma, NSCLC, CRC, and other malignancies that harbor this mutation. In preclinical studies, CFT1946 is active *in vivo* and *in vitro* in models with BRAF V600E-driven disease and in models resistant to BRAF inhibitors. In January 2023, we initiated a first-in-human Phase 1/2 clinical trial of CFT1946 for the treatment of BRAF V600 mutant solid tumors including NSCLC, colorectal cancer and melanoma, and continue to enroll patients in the Phase 1 dose escalation portion of the trial.

Additionally, we are developing CFT8919, an orally bioavailable, allosteric, mutant-selective BiDAC degrader of epidermal growth factor receptor, or EGFR, with an L858R mutation in NSCLC. In preclinical studies, CFT8919 demonstrated equipotent activity against EGFR mutations resistant to EGFR inhibition, including L858R-C797S, L858R-T790M, and L858R-T790M-C797S compared to L858R single mutation in Ba/F3 cell models *in vitro*. We completed IND-enabling activities for this program in December 2022.

Beyond these initial product candidates, we are further diversifying our pipeline by developing new degraders against both clinically validated and currently undruggable targets for our own proprietary pipeline and for the pipeline we are developing in collaboration with Roche, Biogen and Calico. We have engineered degraders that have successfully achieved blood-brain barrier penetration in preclinical studies, which is a key step in developing medicines with the potential to treat brain metastases in oncology, as well as in therapeutic areas such neurodegenerative diseases. We also believe there are many other therapeutic areas and indications where leveraging our TORPEDO platform to develop novel degraders may be advantageous.

## **Financial operations overview**

### ***Revenues***

To date, we have not generated any revenue from product sales and do not expect to generate any revenue from the sale of products for the foreseeable future. Our revenues to date have been generated through research collaboration and license agreements. We recognize revenue over the expected performance period under each agreement. We expect that our revenue for the next several years will be derived primarily from our current collaboration agreements and any additional collaborations that we may enter into in the future. To date, we have not received any royalties under any of our existing collaboration agreements.

For a description of our collaboration agreements with F. Hoffman-La Roche Ltd and Hoffiman-La Roche Inc., or Roche, Biogen MA, Inc., or Biogen, and Calico Life Sciences LLC, or Calico, please see Note 8, *Collaboration and license agreements*, to the consolidated financial statements in this Annual Report on Form 10-K.

### ***Research and development expenses***

Research and development expenses consist primarily of costs incurred for our research activities, including our discovery efforts, and the development of our product candidates, and include:

- salaries, benefits, and other related costs, including stock-based compensation expense, for personnel engaged in research and development functions;
- expenses incurred under agreements with third parties, including contract research organizations and other third parties that conduct research, preclinical, and clinical activities on our behalf as well as third parties that manufacture our product candidates for use in our preclinical and clinical trials;
- costs of outside consultants, including their fees, and related travel expenses;
- the costs of laboratory supplies and acquiring materials for preclinical studies and clinical trials;
- facility-related expenses, which include direct depreciation costs of equipment and allocated expenses for rent and maintenance of facilities and other operating costs; and
- third-party licensing fees.

We expense research and development costs as incurred. Costs for external development activities are recognized based on an evaluation of the progress to completion of specific tasks using information provided to us by our vendors. Payments for these activities are based on the terms of the individual agreements, which may differ from the pattern of costs incurred, and are reflected in our consolidated financial statements as prepaid or accrued research and development expenses. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are recorded as prepaid expenses and expensed as the related goods are delivered or the services are performed.

We expect that our research and development expenses will continue to increase substantially in connection with our planned preclinical and clinical development activities.

### ***General and administrative expenses***

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in our executive, finance, legal, business development, and administrative functions. General and administrative expenses also include legal fees relating to corporate matters; professional fees for accounting, auditing, tax and consulting services; insurance costs; travel expenses; and facility-related expenses, which include direct depreciation costs and allocated expenses for rent and maintenance of facilities and other operating costs.

We expect that our general and administrative expenses will continue to increase in the future to support increased research and development activities. These increases will likely include higher costs related to the hiring of additional personnel; fees to outside consultants, lawyers, and accountants; and investor and public relations costs.

### ***Other income (expense)***

Other income (expense), net primarily consists of the following:

- interest expense and amortization of our long-term debt; and
- interest and other income earned on our cash, cash equivalents, and marketable securities and accretion of discount on marketable securities.

**Results of operations****Comparison of years ended December 31, 2022 and 2021***Revenue*

Revenue from our collaboration and license agreements consisted of the following (in thousands):

	Years Ended December 31,	
	2022	2021
Revenue from collaboration agreements:		
Biogen Agreement	\$ 19,214	\$ 15,720
Calico Agreement	6,943	10,686
Roche Agreement	4,939	19,379
Total revenue from collaboration agreements	<u>\$ 31,096</u>	<u>\$ 45,785</u>

The \$14.7 million decrease in revenue in the year ended December 31, 2022 as compared to the year ended December 31, 2021 is primarily driven by:

- a \$14.4 million decrease in revenue recognized under the Roche Agreement primarily as a result of the termination of the Roche Agreement as to the BRAF target; and
- a \$3.7 million decrease in revenue recognized under the Calico Agreement, primarily driven by a decrease in full-time equivalent, or FTE, reimbursements and the impact of the one-year extension of the term of the Calico Agreement's with respect to one of the research programs in that collaboration.

These were offset by a \$3.5 million increase in revenue recognized under the Biogen Agreement, primarily driven by continued progress against the nominated targets and the achievement of an additional Biogen Agreement milestone in 2022.

*Research and Development Expenses*

The following table summarizes our research and development expenses (in thousands):

	Years Ended December 31,	
	2022	2021
Research and development expenses:		
Preclinical and development expenses	\$ 42,033	\$ 46,012
Personnel expenses	41,068	29,142
Facilities and supplies	13,978	8,805
Clinical expenses	10,643	2,661
Professional fees	7,047	5,625
Intellectual property	2,493	2,108
Other expenses	579	312
Total research and development expenses	<u>\$ 117,841</u>	<u>\$ 94,665</u>

The \$23.2 million increase in research and development expense in the year ended December 31, 2022 from the year ended December 31, 2021 is primarily driven by:

- a \$11.9 million increase in personnel expenses, representing salary and benefit costs, including a \$5.6 million increase in stock-based compensation expense, driven primarily by the build-out of our clinical development team to support a greater number of clinical-stage programs;
- a \$8.0 million increase in clinical costs resulting from the ongoing Phase 1/2 clinical trials of CFT7455 and CFT8634, and start up activities related to our clinical trial of CFT1946;
- a \$5.2 million increase in facilities and supplies costs, primarily driven by our additional leased space; and
- a \$1.4 million increase in professional fees, which primarily consists of consulting costs for our development activities.

These were offset by a \$4.0 million decrease in preclinical and development costs related to additional programs progressing to clinical stages.

#### *General and Administrative Expenses*

The following table summarizes our general and administrative expenses (in thousands):

	Years Ended December 31,	
	2022	2021
<b>General and administrative expenses:</b>		
Personnel expenses	\$ 30,546	\$ 23,013
Professional fees	8,576	8,781
Facilities and supplies	2,371	548
Other expenses	1,296	912
<b>Total general and administrative expenses</b>	<b>\$ 42,789</b>	<b>\$ 33,254</b>

The \$9.5 million increase in general and administrative expense in the year ended December 31, 2022 as compared to the year ended December 31, 2021 is primarily driven by:

- a \$7.5 million increase in personnel expenses, representing salary and benefit costs, including a \$4.3 million increase in salaries and wages, mainly driven by the full-year 2022 impact of the build-out of our general and administrative team, including our executive team and Business Development function, and a \$2.9 million increase in stock-based compensation; and
- a \$1.8 million increase in facilities and supplies, which is primarily driven by our additional leased space.

#### *Other Income (Expenses)*

The following table summarizes our other income (expense) (in thousands):

	Years Ended December 31,	
	2022	2021
<b>Other income (expense), net</b>		
Interest expense and amortization of long-term debt—related party	\$ (2,216)	\$ (2,145)
Interest and other income, net	3,575	387
<b>Total other income (expense), net</b>	<b>\$ 1,359</b>	<b>\$ (1,758)</b>

The \$3.1 million increase in other income (expense) for the year ended December 31, 2022 as compared to the year ended December 31, 2021 was driven by a \$3.2 million increase in interest and other income resulting from higher interest earned on our investments during 2022.

### **Liquidity and capital resources**

#### *Sources of liquidity*

Since inception, we have incurred significant operating losses. We expect to incur significant expenses and operating losses for the foreseeable future as we continue development of our programs. We do not currently have any approved products and have never generated any revenue from product sales. To date, we have financed our operations primarily through the sale of preferred stock, public offerings of our common stock, and payments from collaboration partners. As of December 31, 2022, we had cash, cash equivalents and marketable securities of approximately \$337.1 million.

In June 2021, we completed a follow-on public offering, at which time we sold 4,887,500 shares of our common stock, which number includes 637,500 shares of common stock that were issued to the underwriters when they exercised in full their overallotment option. Net proceeds from the follow-on offering, including the exercise in full of the underwriters' option to purchase additional shares, were \$169.5 million, after deducting underwriting discounts and commissions, and expenses of \$11.3 million.

In November 2021, we filed an automatically effective registration statement on Form S-3, or the Registration Statement, with the SEC which registers the offering, issuance, and sale of an unspecified amount of common stock, preferred stock, debt securities, warrants, and/or units of any combination thereof. We simultaneously entered into an equity distribution agreement with Cowen and Company, LLC, as sales agent, to provide for the issuance and sale by us of up to \$200.0 million of common stock from time to time in "at-the-market" offerings under the Registration Statement and related

prospectus filed with the Registration Statement, or the ATM Program. As of December 31, 2022, we have not made any sales under the ATM Program.

### **Cash flows**

The following table summarizes our sources and uses of cash for the period presented (in thousands):

	Years Ended December 31,	
	2022	2021
Net change in cash, cash equivalents and restricted cash:		
Net used in operating activities	\$ (105,939)	\$ (86,965)
Net cash provided by (used in) investing activities	58,422	(189,336)
Net cash provided by financing activities	1,147	171,400
Net change in cash, cash equivalents and restricted cash	<u>\$ (46,370)</u>	<u>\$ (104,901)</u>

#### *Operating activities*

Net cash used in operating activities for the year ended December 31, 2022 was driven primarily by:

- our net loss of \$128.2 million;
- a \$22.7 million change in deferred revenue due to the recognition of revenue under our collaboration agreements; and
- a \$3.3 million change in accounts payable.

These amounts were offset by:

- a \$37.6 million of non-cash expense related to stock compensation expense, depreciation and amortization, and reduction in carrying amount of our right-of-use asset;
- a \$5.1 million change in accrued expenses and other current liabilities; and
- a \$4.2 million change in accounts receivable.

Net cash used in operating activities for the year ended December 31, 2021 was driven primarily by:

- our net loss of \$83.9 million;
- a \$25.1 million change in deferred revenue due to the recognition of revenue under our collaboration agreements;
- a \$6.1 million change in prepaid expenses and other current assets;
- a \$1.2 million change in accounts receivable; and
- a \$1.2 million change in accounts payable.

These amounts were offset by:

- a \$26.3 million of non-cash expense related to stock compensation expense, depreciation, accretion of discount on investments, and reduction in carrying amount of our right-of-use asset; and
- a \$4.4 million change in accrued expenses and other liabilities.

#### *Investing activities*

The \$58.4 million of net cash provided by investing activities for the year ended December 31, 2022 was attributable to \$63.9 million for the proceeds from maturities of marketable securities, net of purchases, and was offset by \$5.5 million for the purchases of property and equipment.

The \$189.3 million of net cash used in investing activities for the year ended December 31, 2021 was attributable to:

- \$188.1 million for the purchases of marketable securities, net of maturities; and
- \$1.3 million for the purchases of property and equipment.



### *Financing activities*

The \$1.1 million of net cash provided by financing activities for the year ended December 31, 2022 is primarily driven by proceeds from exercises of stock options.

The \$171.4 million of net cash provided by financing activities for the year ended December 31, 2021 is primarily driven by:

- \$169.5 million of proceeds from our follow-on offering, net of issuance costs paid; and
- \$2.3 million of proceeds from exercises of stock options.

### *Funding requirements*

Since our inception, we have incurred significant operating losses and we expect to continue to incur significant expenses and increasing operating losses for the foreseeable future as we advance the preclinical and clinical development of our product candidates. In addition, we expect to continue to incur costs associated with operating as a public company.

Specifically, we anticipate that our expenses will increase substantially in the future, if and as we:

- continue our ongoing first-in-human Phase 1/2 trials and initiate and conduct planned first-in-human Phase 1/2 trials for our other lead product candidates;
- advance additional product candidates into preclinical and clinical development;
- continue to invest in our proprietary TORPEDO platform;
- advance, expand, maintain, and protect our intellectual property portfolio;
- hire additional clinical, regulatory, quality, and scientific personnel;
- add operational, financial and management information systems and personnel to support our ongoing research, product development, potential future commercialization efforts, operations as a public company, and general and administrative roles;
- seek marketing approvals for any product candidates that successfully complete clinical trials; and
- ultimately establish a sales, marketing and distribution infrastructure, and scale up external manufacturing capabilities to commercialize any products for which we may obtain marketing approval.

Because of the numerous risks and uncertainties associated with development and commercialization of our product candidates, we are unable to estimate the amounts of increased capital and operating costs associated with our current and anticipated preclinical and clinical development. Our future capital requirements will depend on many factors, including:

- the progress, costs and results of ongoing and planned first-in-human Phase 1/2 trials for our lead product candidates, and any future clinical development of those lead product candidates;
- the scope, progress, costs and results of preclinical and clinical development for our other product candidates, and development programs;
- the number and development requirements of other product candidates that we pursue;
- the progress and success of our collaborations with Roche, Biogen, and Calico, including whether or not we receive additional research support or milestone payments from our collaboration partners upon the achievement of milestones;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs and timing of preparing, filing, and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims;
- our willingness and ability to establish additional collaboration arrangements with other biotechnology or pharmaceutical companies on favorable terms, if at all, for the development or commercialization of current or additional future product candidates;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval; and
- the revenue, if any, received from commercial sales of our product candidates for which we receive marketing approval.

As a result of the anticipated expenditures described above, we will need to obtain substantial additional financing to support our continuing operations and pursue our long-term business plan. Until such time, if ever, that we can generate substantial revenue from product sales, we expect to finance our cash needs through a combination of equity offerings, debt offerings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. Although we may receive potential future milestone and royalty payments under our collaborations with Roche, Biogen, and Calico, we do not have any committed external source of funds as of December 31, 2022. Adequate additional funds may not be available to us on acceptable terms, or at all. If we are unable to raise capital when needed or on attractive terms, we may be required to delay, limit, reduce or terminate our research, 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.

If we raise additional capital through the sale of equity securities, each investor's 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. Preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as making acquisitions or capital expenditures or declaring dividends.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us.

### **Contractual obligations**

The following is a summary of our significant contractual obligations as of December 31, 2022 (in thousands):

	Total	Less than 1 Year	1 to 3 Years	4 to 5 Years	More than 5 Years
<b>Contractual obligations:</b>					
Operating lease commitments (see Note 6)	\$ 97,617	\$ 8,571	\$ 17,921	\$ 19,012	\$ 52,113
Long-term debt (see Note 9)	12,500	3,000	9,500	—	—
<b>Total contractual obligations</b>	<b>\$ 110,117</b>	<b>\$ 11,571</b>	<b>\$ 27,421</b>	<b>\$ 19,012</b>	<b>\$ 52,113</b>

We enter into contracts in the normal course of business with third-party CROs for clinical trials, preclinical studies, manufacturing and other services, and products for operating purposes. These contracts generally provide for termination following a certain period after notice and therefore we believe that our non-cancelable obligations under these agreements are not material, and they are not included in the table above. We have not included milestone or royalty payments or other contractual payment obligations in the table above if the timing and amount of such obligations are unknown or uncertain.

### **Critical accounting estimates**

This management's discussion and analysis of financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with generally accepted accounting principles in the United States. The preparation of our consolidated financial statements and related disclosures requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities, revenues, costs and expenses, and the disclosure of contingent assets and liabilities in our consolidated financial statements. We base our estimates on historical experience, known trends and events and various other factors that we believe are 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. We evaluate our estimates and assumptions on an ongoing basis. Our actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in Note 2, *Summary of significant accounting policies*, to our consolidated financial statements in this Annual Report on Form 10-K, we believe that the following accounting policies are those most critical to the judgments and estimates used in the preparation of our consolidated financial statements.

### **Revenues from contracts**

We account for our revenue in accordance with Accounting Standards Codification, or ASC, 606, *Revenue from Contracts with Customers*, or ASC 606. Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration that the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs the following five steps at inception of the agreement or upon material modification of the agreement: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the

transaction price, including variable consideration, if any; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation.

We consider the pattern of satisfaction of the performance obligations under step (v) above to be a critical accounting estimate. More specifically, the determination of the level of achievement of research and development service performance obligations, whose pattern of satisfaction is measured using costs incurred to date as compared to total costs incurred and expected to be incurred in the future is driven by a critical accounting estimate.

In estimating the costs expected to be incurred in the future, management uses its most recent budget and long-range plan, adjusted for any pertinent information. While this is our best estimate as of the reporting period, costs expected to be incurred in the future require management judgment as the scope and timing of research and development activities may change significantly over time. We may adjust the scope of our research and development activities based on several factors, such as additional work needed to support advancement of product candidate or change in the number of patients in trials. Further, research and development services may no longer be within the scope of a collaboration agreement, as has been the case with certain of our programs. The timing of when research and development costs are expected to be incurred may change as a result of external factors, such as delays caused by manufacturing or supply chain, or difficulty in enrolling patients; or internal factors, such as prioritization of programs. Our estimate of the scope and timing of research and development services performed relative to the actual scope and timing may have a significant impact on revenue recognition.

#### ***Prepaid and accrued research and development expenses***

As part of preparing our consolidated financial statements, we are required to estimate our accrued research and development expenses. This process involves reviewing quotations and contracts, identifying services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. We make estimates of the accrued expenses as of each balance sheet date in our consolidated financial statements based on facts and circumstances known to us at that time. In addition, there may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the expense, in which case such amounts are reflected as prepaid expenses and other current assets. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or the amount of prepaid expenses accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and could have a significant impact on reported amounts.

Non-refundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized in prepaid expenses and other current assets. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

#### ***Operating leases (incremental borrowing rate)***

We account for leases in accordance with ASC Topic 842, *Leases*, or ASC 842. Under ASC 842, at inception or upon modification of a lease arrangement, we may be required to remeasure our lease liabilities and the corresponding right-of-use assets. The lease liability is measured by calculating the present value of lease payments under the lease arrangement using the incremental borrowing rate. Incremental borrowing rate is the rate of interest that we would have to pay to borrow, on a collateralized basis, an amount equal to the lease payments over a similar term equal to the lease term in a similar economic environment.

Since the incremental borrowing rates implicit in our leases are not readily determinable, we use the estimated incremental borrowing rates based on the information available at commencement date in determining the discount rate used to calculate the present value of lease payments. As we have no recent external borrowings, the incremental borrowing rates are determined using information on indicative borrowing rates that would be available to us based on the value and borrowing term provided by financial institutions, adjusted for company and market specific factors. This determination requires management judgement, including when determining peer groups, our own risk profile, and when adjusting for company and market specific factors.

Although we do not expect our estimates of the incremental borrowing rates to generate material differences within a reasonable range of sensitivities, judgement is involved in selecting an appropriate rate, and the rate selected for our leases will have an impact on the value of the lease liability and corresponding right-of-use asset in the consolidated balance sheets.

### ***Stock options***

We account for all stock-based awards granted to employees and non-employees as stock-based compensation expense at fair value. Our stock-based payments include stock options, restricted stock units, and grants of common stock, including common stock subject to vesting. The measurement date for awards is the date of grant, and stock-based compensation costs are recognized as expense over the requisite service period, which is generally the vesting period, on a straight-line basis. Stock-based compensation expense is classified in the consolidated statements of operations and comprehensive loss based on the function to which the related services are provided. We recognize stock-based compensation expense for the portion of awards that have vested. Forfeitures are recorded as they occur. The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option pricing model. The Black-Scholes option pricing model includes various assumptions, including the expected term of the award, the expected volatility and the expected risk-free interest rate over the expected term of the award, expected dividend payments, and the fair value of the common stock underlying the stock-based award.

We consider the expected volatility to be a critical accounting estimate. As we do not have sufficient trading history, we use the average historical volatility of a representative group of publicly traded biopharmaceutical companies, including our own, to calculate the expected volatility for use in the Black-Scholes option pricing model. This assumption reflects our best estimate, but it involves inherent uncertainties based on market conditions generally outside our control. As a result, if a different volatility had been used, stock-based compensation cost could have been materially impacted.

### ***New accounting pronouncements***

We became a smaller reporting company on December 31, 2022 based on the market value of our common stock held by non-affiliates as of the last day of the second quarter in 2022. Prior to that, we were a large accelerated filer as of December 31, 2021.

We gained the ability to delay adoption of new or revised accounting pronouncements when we became a smaller reporting company as of December 31, 2022. For information on new accounting standards, see Note 2, *Summary of significant accounting policies*, to our consolidated financial statements in this Annual Report on Form 10-K.

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

We are exposed to market risks in the ordinary course of our business. These risks primarily include interest rate sensitivities. Our interest-earning assets consist of cash, cash equivalents, and marketable securities. Our interest income is sensitive to changes in the general level of interest rates, primarily United States interest rates. As of December 31, 2022, we had marketable securities of \$307.4 million. Our marketable securities are short-term in nature with a weighted-average maturity date of 0.6 years. As such, while these interest-earning instruments carry a degree of interest rate risk, historical fluctuations in interest income have not been significant for us.

### **Item 8. Financial Statements and Supplementary Data.**

The financial statements required to be filed pursuant to this Item 8 are appended to this Annual Report on Form 10-K. An index of those financial statements is found in Item 15, *Exhibits and Financial Statement Schedules*, of this Annual Report on Form 10-K.

### **Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure.**

None.

### **Item 9A. Controls and Procedures.**

#### *Evaluation of Disclosure Controls and Procedures*

Our management, with the participation of our principal executive officer and our principal financial officer, evaluated, as of the end of the period covered by this Annual Report on Form 10-K, the effectiveness of our disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act. The term “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC’s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company’s management, including its principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only

reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

Based on the evaluation of our disclosure controls and procedures as of December 31, 2022, our principal executive officer and principal financial officer concluded that our disclosure controls and procedures as of such date are effective at the reasonable assurance level.

*Management's Annual Report on Internal Control over Financial Reporting*

Our management is responsible for establishing and maintaining adequate internal control over our financial reporting. Internal control over financial reporting is defined in Rules 13a-15(f) and 15d-15(f) promulgated under the Exchange Act as a process designed by, or under the supervision of, our principal executive and principal financial officers and effected by our board of directors, management, and other personnel to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with United States GAAP. Our internal control over financial reporting includes those policies and procedures that:

- pertain to the maintenance of records that, in reasonable detail, accurately, and fairly reflect our transactions and dispositions of our assets;
- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with United States GAAP, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors; and
- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on our financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. 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. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission, or COSO, in its 2013 Internal Control – Integrated Framework. Based on our assessment, our management has concluded that, as of December 31, 2022, our internal control over financial reporting is effective based on those criteria.

*Changes in Internal Control over Financial Reporting*

We continuously seek to improve the efficiency and effectiveness of our internal controls. This results in refinements to processes throughout the company. There were no changes in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the year ended December 31, 2022 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

*Inherent Limitations on Effectiveness of Controls*

The effectiveness of any system of internal control over financial reporting, including ours, is subject to inherent limitations, including the exercise of judgment in designing, implementing, operating, and evaluating the controls and procedures, and the inability to eliminate misconduct completely. Accordingly, any system of internal control over financial reporting, including ours, no matter how well designed and operated, can only provide reasonable, not absolute assurances. In addition, 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. We intend to continue to monitor and upgrade our internal controls as necessary or appropriate for our business, but there can be no assurance that such improvements will be sufficient to provide us with effective internal control over financial reporting. See “Risk Factors—*We will continue to incur additional costs as a result of operating as a public company and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices.*”

**Item 9B. Other Information.**

None.

**Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.**

None.

### PART III

**Item 10. Directors, Executive Officers and Corporate Governance.**

The information required by this Item 10 will be included in our definitive proxy statement to be filed with the Securities and Exchange Commission, or SEC, with respect to our 2023 Annual Meeting of Stockholders within 120 days after the end of the year covered by this Annual Report on Form 10-K and is incorporated herein by reference.

**Item 11. Executive Compensation.**

The information required by this Item 11 will be included in our definitive proxy statement to be filed with the SEC within 120 days after the end of the year covered by this Annual Report on Form 10-K with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

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

The information required by this Item 12 will be included in our definitive proxy statement to be filed with the SEC within 120 days after the end of the year covered by this Annual Report on Form 10-K with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

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

The information required by this Item 13 will be included in our definitive proxy statement to be filed with the SEC within 120 days after the end of the year covered by this Annual Report on Form 10-K with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

**Item 14. Principal Accounting Fees and Services.**

The information required by this Item 14 will be included in our definitive proxy statement to be filed with the SEC within 120 days after the end of the year covered by this Annual Report on Form 10-K with respect to our 2023 Annual Meeting of Stockholders and is incorporated herein by reference.

## PART IV

**Item 15. Exhibits, Financial Statement Schedules.***1. Financial Statements*

For a list of the financial statements included herein, see *Index to the Consolidated Financial Statements* on page F-1 of this Annual Report on Form 10-K, incorporated into this Item by reference.

*2. Financial Statement Schedules*

Financial statement schedules have been omitted because they are either not required or not applicable or the information is included in the consolidated financial statements or the notes thereto.

*3. Exhibits*

Exhibit Number	Description of Exhibit	Form	File Number	Date of Filing	Exhibit Number	Filed Herewith
3.1	<a href="#">Fifth Amended and Restated Certificate of Incorporation of the Registrant, current in effect</a>	8-K	001-39567	10/06/2020	3.3	
3.2	<a href="#">Form of Second Amended and Restated Bylaws of the Registrant</a>	S-1	333-248719	09/10/2020	3.5	
4.1	<a href="#">Amended and Restated Investors' Rights Agreement among the Registrant, its warrant holder and certain of its stockholders, dated June 5, 2020</a>	S-1	333-248719	09/10/2020	4.1	
4.2	<a href="#">Form of Specimen Common Stock Certificate</a>	S-1/A	333-248719	09/28/2020	4.3	
4.3	<a href="#">Description of Securities Registered Pursuant to Section 12 of the Securities Exchange Act of 1934, as amended</a>	10-K	001-39567	03/11/2021	4.4	
10.1#	<a href="#">2015 Stock Option and Grant Plan, as amended and forms of award agreements thereunder</a>	S-1	333-248719	09/10/2020	10.1	
10.2#	<a href="#">2020 Stock Option and Incentive Plan and forms of award agreements thereunder</a>					X
10.3#	<a href="#">2020 Employee Stock Purchase Plan</a>	S-1/A	333-248719	09/28/2020	10.3	
10.4#	<a href="#">Senior Executive Cash Incentive Bonus Plan</a>	S-1	333-248719	09/10/2020	10.4	
10.5#	<a href="#">Form of Director Indemnification Agreement</a>	S-1	333-248719	09/10/2020	10.5	
10.6#	<a href="#">Form of Officer Indemnification Agreement</a>	S-1	333-248719	09/10/2020	10.6	
10.7#	<a href="#">Form of Executive Employment Agreement</a>	S-1	333-248719	09/10/2020	10.7	
10.8#	<a href="#">Employment Agreement between the Registrant and Andrew Hirsch, dated September 6, 2020</a>	S-1	333-248719	09/10/2020	10.8	
10.9†	<a href="#">Collaboration Research and License Agreement between the Registrant and Biogen MA, Inc., dated December 28, 2018</a>	S-1	333-248719	09/10/2020	10.10	
10.10†	<a href="#">Amendment No. 1 to Collaborative Research and License Agreement between the Registrant and Biogen MA, Inc., dated February 25, 2020</a>	10-K	001-39567	03/11/2021	10.11	
10.11†	<a href="#">Amended and Restated License Agreement among the Registrant, F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc., dated December 20, 2018</a>	S-1	333-248719	09/10/2020	10.11	

## Table of Contents

<b>Exhibit Number</b>	<b>Description of Exhibit</b>	<b>Form</b>	<b>File Number</b>	<b>Date of Filing</b>	<b>Exhibit Number</b>	<b>Filed Herewith</b>
10.12†	<a href="#">First Amendment to the Amended and Restated License Agreement among the Registrant, F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc., dated November 12, 2020</a>	10-K	001-39567	03/11/2021	10.13	
10.13†	<a href="#">Collaboration and License Agreement between the Registrant and Calico Life Sciences LLC, dated March 13, 2017</a>	S-1	333-248719	09/10/2020	10.12	
10.14†	<a href="#">Credit Agreement and Guaranty among the Registrant, Perceptive Credit Holdings III, LP and the guarantors and lenders party thereto, dated July 5, 2020</a>	S-1	333-248719	09/10/2020	10.13	
10.15	<a href="#">Lease by 480 Arsenal Group LLC to the Registrant, dated July 5, 2017, as amended</a>	S-1	333-248719	09/10/2020	10.14	
10.16	<a href="#">Third Amendment to Lease, dated November 24, 2021, by and between C4 Therapeutics, Inc. and Columbia Massachusetts Arsenal Office Properties, LLC</a>	8-K	001-39567	11/30/2021	10.1	
21.1	<a href="#">Subsidiaries of the Registrant</a>					X
23.1	<a href="#">Consent of KPMG LLP, Independent Registered Public Accounting Firm</a>					X
31.1	<a href="#">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</a>					X
31.2	<a href="#">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</a>					X
32.1*	<a href="#">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</a>					X
32.2*	<a href="#">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</a>					X
101.INS	Inline XBRL Instance Document					X
101.SCH	Inline XBRL Taxonomy Extension Schema Document					X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document					X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document					X
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document					X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document					X



## [Table of Contents](#)

<b>Exhibit Number</b>	<b>Description of Exhibit</b>	<b>Form</b>	<b>File Number</b>	<b>Date of Filing</b>	<b>Exhibit Number</b>	<b>Filed Herewith</b>
104	Cover Page Interactive Data File (formatted as Inline XBRL document and contained in Exhibit 101)					

---

# Indicates a management contract or any compensatory plan, contract or arrangement.

† Portions of this exhibit (indicated by asterisks) will be omitted in accordance with the rules of the Securities and Exchange Commission.

\* Exhibits 32.1 and 32.2 are being furnished and shall not be deemed to be “filed” for purposes of Section 18 of the Exchange Act, or otherwise subject to the liability of that section, nor shall such exhibit be deemed to be incorporated by reference in any registration statement or other document filed under the Securities Act, or the Exchange Act, except as otherwise stated in such filing.

### **Item 16. Form 10-K Summary**

Not applicable.



**INDEX TO CONSOLIDATED FINANCIAL STATEMENTS**

<a href="#">Report of Independent Registered Public Accounting Firm</a>	F-2
<a href="#">Consolidated Balance Sheets</a>	F-4
<a href="#">Consolidated Statements of Operations and Comprehensive Loss</a>	F-5
<a href="#">Consolidated Statements of Stockholders' Equity</a>	F-6
<a href="#">Consolidated Statements of Cash Flows</a>	F-7
<a href="#">Notes to Consolidated Financial Statements</a>	F-9

## Report of Independent Registered Public Accounting Firm

To the Stockholders and Board of Directors

C4 Therapeutics, Inc.:

### *Opinion on the Consolidated Financial Statements*

We have audited the accompanying consolidated balance sheets of C4 Therapeutics, Inc. and subsidiary (the Company) as of December 31, 2022 and 2021, the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows for each of the years in the two-year period ended December 31, 2022, and the related notes (collectively, the consolidated financial statements). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the years in the two-year period ended December 31, 2022, in conformity with U.S. generally accepted accounting principles.

### *Basis for Opinion*

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

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

### *Critical Audit Matter*

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the consolidated financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of a critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

#### *Evaluation of revenue recognition for certain research and development services*

As discussed in Notes 2 and 8 to the consolidated financial statements, the Company is party to collaboration agreements which have various performance obligations, including the promise to perform research and development (R&D) services on behalf of the customer. For certain collaboration agreements, the Company recognizes revenue for the portion of the transaction price allocated to each of the R&D performance obligations as the R&D services are provided, using an input method, according to costs incurred as related to the research and development activities for each individual program and the costs expected to be incurred in the future to satisfy that individual performance obligation. Amounts received by the Company prior to satisfying the revenue recognition criteria are recorded as deferred revenue. For the year ended December 31, 2022, the Company recognized revenue from collaboration agreements of \$31.1 million, a portion of which related to R&D services performed. In addition, as of December 31, 2022, a portion of the Company's current and net of current deferred revenue related to R&D services to be performed.

We identified the evaluation of revenue recognition for certain R&D services as a critical audit matter. Specifically, evaluating the estimate of total contract costs expected to be incurred in satisfying certain R&D performance obligations, including the assessment of the nature of the work to be performed and the method for measuring progress, involved especially challenging auditor judgment.

The following are the primary procedures we performed to address this critical audit matter. For a selection of R&D performance obligations, we evaluated the estimate of total contract costs expected to be incurred by:

- inspecting the underlying contract with the customer to gain an understanding of the nature of the work to be performed and to evaluate the Company's method for measuring progress
- comparing the Company's prior period estimates to actual costs incurred to assess the Company's ability to estimate accurately
- inspecting underlying documentation and third-party evidence and comparing them to management's assumptions
- inquiring of R&D personnel of the Company to evaluate factors related to the nature of the work to be performed and their impact on the total contract costs to be incurred, including progress to date and the estimate of remaining contract costs.

/s/ KPMG LLP

We have served as the Company's auditor since 2016.

Boston, Massachusetts

February 23, 2023

**C4 Therapeutics, Inc.**  
**Consolidated Balance Sheets**  
(in thousands, except share and per share amounts)

	December 31,	
	2022	2021
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 29,754	\$ 76,124
Marketable securities, current	246,399	233,155
Accounts receivable	1,473	5,716
Prepaid expenses and other current assets	9,931	10,694
<b>Total current assets</b>	<b>287,557</b>	<b>325,689</b>
Marketable securities, non-current	60,962	142,200
Property and equipment, net	7,400	3,108
Right-of-use asset	70,116	31,945
Restricted cash	3,279	3,279
Other assets	1,526	544
<b>Total assets</b>	<b>\$ 430,840</b>	<b>\$ 506,765</b>
<b>Liabilities and stockholders' equity</b>		
Current liabilities:		
Accounts payable	\$ 1,172	\$ 4,506
Accrued expenses and other current liabilities	19,769	13,606
Deferred revenue, current	16,618	31,800
Operating lease liability, current	4,700	1,334
Long-term debt, net of debt discount—related party, current	2,287	—
<b>Total current liabilities</b>	<b>44,546</b>	<b>51,246</b>
Deferred revenue, net of current	16,895	24,368
Operating lease liability, net of current	70,970	30,777
Long-term debt, net of debt discount—related party, net of current	9,195	10,768
<b>Total liabilities</b>	<b>141,606</b>	<b>117,159</b>
Commitments and contingencies (See Note 6 and Note 9)		
Stockholders' equity:		
Preferred stock, par value of \$0.0001 per share; 10,000,000 shares authorized, and no shares issued or outstanding as of December 31, 2022 and 2021, respectively	—	—
Common stock, par value of \$0.0001 per share; 150,000,000 shares authorized, and 48,966,216 and 48,688,875 shares issued and outstanding as of December 31, 2022 and 2021, respectively	5	5
Additional paid-in capital	689,256	658,091
Accumulated other comprehensive loss	(4,137)	(775)
Accumulated deficit	(395,890)	(267,715)
<b>Total stockholders' equity</b>	<b>289,234</b>	<b>389,606</b>
<b>Total liabilities and stockholders' equity</b>	<b>\$ 430,840</b>	<b>\$ 506,765</b>

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

**C4 Therapeutics, Inc.**  
**Consolidated Statements of Operations and Comprehensive Loss**  
**(in thousands, except share and per share amounts)**

	Years Ended December 31,	
	2022	2021
Revenue from collaboration agreements	\$ 31,096	\$ 45,785
Operating expenses:		
Research and development	117,841	94,665
General and administrative	42,789	33,254
Total operating expenses	<u>160,630</u>	<u>127,919</u>
Loss from operations	(129,534)	(82,134)
Other income (expense), net		
Interest expense and amortization of long-term debt—related party	(2,216)	(2,145)
Interest and other income, net	3,575	387
Total other income (expense), net	<u>1,359</u>	<u>(1,758)</u>
Net loss	<u>\$ (128,175)</u>	<u>\$ (83,892)</u>
Net loss per share - basic and diluted	<u>\$ (2.62)</u>	<u>\$ (1.82)</u>
Weighted-average number of shares - basic and diluted	<u>48,861,665</u>	<u>46,041,733</u>
Other Comprehensive loss:		
Unrealized loss on marketable securities	(3,362)	(788)
Comprehensive loss	<u>\$ (131,537)</u>	<u>\$ (84,680)</u>

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

**C4 Therapeutics, Inc.**  
**Consolidated Statements of Stockholders' Equity**  
(in thousands, except share amounts)

	Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balance as of December 31, 2020	43,059,632	\$ 4	\$ 464,597	\$ 13	\$ (183,823)	\$ 280,791
Follow-on common stock offering, net of issuance costs of \$11.3 million	4,887,500	1	169,464	—	—	169,465
Shares issued upon warrant exercise—related party	256,038	—	—	—	—	—
Exercise of stock options	474,850	—	2,330	—	—	2,330
Issuance of common stock under the 2020 ESPP	6,640	—	180	—	—	180
Stock-based compensation	—	—	21,340	—	—	21,340
Unrealized loss on marketable securities	—	—	—	(788)	—	(788)
Net loss	—	—	—	—	(83,892)	(83,892)
Other	4,215	—	180	—	—	180
Balance as of December 31, 2021	48,688,875	\$ 5	\$ 658,091	\$ (775)	\$ (267,715)	\$ 389,606
Exercise of stock options and release of stock units	235,450	—	777	—	—	777
Issuance of common stock under the 2020 ESPP	31,402	—	372	—	—	372
Stock-based compensation	—	—	29,858	—	—	29,858
Unrealized loss on marketable securities	—	—	—	(3,362)	—	(3,362)
Net loss	—	—	—	—	(128,175)	(128,175)
Other	10,489	—	158	—	—	158
Balance as of December 31, 2022	48,966,216	\$ 5	\$ 689,256	\$ (4,137)	\$ (395,890)	\$ 289,234

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



**C4 Therapeutics, Inc.**  
**Consolidated Statements of Cash Flows**  
(in thousands)

	Years Ended December 31,	
	2022	2021
Cash flows used in operating activities:		
Net loss	\$ (128,175)	\$ (83,892)
Adjustments to reconcile net loss to cash used in operating activities:		
Stock-based compensation expense	30,016	21,512
Depreciation and amortization	1,676	1,492
Reduction in carrying amount of right-of-use asset	5,896	1,415
Accretion of discount on marketable securities	714	1,879
Amortization of debt discount—related party	713	719
Changes in operating assets and liabilities:		
Accounts receivable	4,244	(1,232)
Prepaid expenses and other current and long-term assets	388	(6,116)
Accounts payable	(3,333)	(1,179)
Accrued expenses and other current liabilities	5,083	4,377
Operating lease liability	(507)	(888)
Deferred revenue	(22,654)	(25,052)
Net cash used in operating activities	(105,939)	(86,965)
Cash flows provided by (used in) investing activities:		
Proceeds from maturities of marketable securities	283,445	349,681
Purchase of marketable securities	(219,527)	(537,740)
Purchases of property and equipment	(5,496)	(1,277)
Net cash provided by (used in) investing activities	58,422	(189,336)
Cash flows provided by financing activities:		
Proceeds from follow-on offering, net of issuance costs paid of \$11.3 million	—	169,465
Proceeds from exercises of stock options	777	2,330
Payment of initial public offering costs	—	(286)
Other	370	(109)
Net cash provided by financing activities	1,147	171,400
Net change in cash, cash equivalents and restricted cash	(46,370)	(104,901)
Cash, cash equivalents and restricted cash at beginning of period	79,403	184,304
Cash, cash equivalents and restricted cash at end of period	\$ 33,033	\$ 79,403
Reconciliation of cash, cash equivalents and restricted cash:		
Cash, cash equivalents and restricted cash at end of year	\$ 33,033	\$ 79,403
Less: restricted cash	(3,279)	(3,279)
Cash and cash equivalents at end of the year	\$ 29,754	\$ 76,124

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

**C4 Therapeutics, Inc.**  
**Consolidated Statements of Cash Flows — Continued**  
**(in thousands)**

	<u>Years Ended December 31,</u>	
	<u>2022</u>	<u>2021</u>
Supplemental disclosure of cash flow information:		
Cash paid for interest - related party	\$ 1,624	\$ 1,308
Supplemental disclosures of non-cash investing and financing activities:		
Operating lease liabilities arising from obtaining right-of-use assets	\$ 44,067	\$ 20,131
Capital expenditures in accounts payable and accrued expenses	\$ 473	\$ —
Aggregate exercise price of warrant net exercised - related party (Note 10)	\$ —	\$ 3,002

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

**C4 Therapeutics, Inc.**  
**Notes to Consolidated Financial Statements**

**Note 1. Nature of the business**

C4 Therapeutics, Inc., or, together with its subsidiary, the Company, is a clinical-stage biopharmaceutical company dedicated to advancing targeted protein degradation science to develop a new generation of small-molecule medicines to transform how disease is treated. C4T leverages its proprietary technology platform, TORPEDO (Target ORiented ProtEIn Degradation Optimizer), to efficiently design and optimize small-molecule medicines that harness the body's natural protein recycling system to rapidly degrade disease-causing protein, offering the potential to overcome drug resistance, drug undruggable targets and improve patient outcomes. C4T uses the TORPEDO platform to advance multiple targeted oncology programs to the clinic while expanding the platform to deliver the next wave of medicines for difficult-to-treat diseases. The Company was incorporated in Delaware on October 7, 2015 and has its principal office in Watertown, Massachusetts.

***Liquidity and capital resources***

Since its inception, the Company's primary activities have been focused on performing research and development activities, building the Company's intellectual property, recruiting personnel, and raising capital to support these activities. To date, the Company has funded its operations primarily with proceeds received from the sales of redeemable convertible preferred stock, public offerings of the Company's common stock, through its collaboration agreements, and debt financing.

The Company has incurred recurring losses since its inception, including net losses of \$128.2 million and \$83.9 million for the years ended December 31, 2022 and 2021, respectively. In addition, as of December 31, 2022, the Company had an accumulated deficit of \$395.9 million. To date, the Company has not generated any revenue from product sales as none of its product candidates has been approved for commercialization. The Company expects to continue to generate operating losses for the foreseeable future.

The Company expects that its cash, cash equivalents, and marketable securities of \$337.1 million as of December 31, 2022 will be sufficient to fund its operations for at least the next twelve months from the date of issuance of these consolidated financial statements. Accordingly, the consolidated financial statements have been prepared on a basis that assumes the Company will continue as a going concern and contemplates the realization of assets and satisfaction of liabilities and commitments in the ordinary course of business.

***Risks and uncertainties***

The Company is subject to risks common to other life science companies in the early development stage including, but not limited to, uncertainty of ability to raise additional financing, product development and commercialization, development by its competitors of new technological innovations, dependence on key personnel, market acceptance of products, lack of marketing and sales history, product liability, protection of proprietary technology and intellectual property, and compliance with the Food and Drug Administration, or the FDA, and other government regulations. If the Company does not successfully advance its programs into and through human clinical trials and commercialize any of its product candidates either directly or through collaborations with other companies, the Company may be unable to produce product revenue or achieve profitability. There can be no assurance that the Company's research and development efforts will be successful, adequate protection for the Company's intellectual property will be obtained, any products developed will obtain necessary government regulatory approval, or any approved products will be commercially viable. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will generate significant revenue from product sales. The Company operates in an environment of rapid change in technology and substantial competition from pharmaceutical and biotechnology companies.

**Note 2. Summary of significant accounting policies**

***Basis of presentation***

The Company has prepared the accompanying consolidated financial statements in conformity with generally accepted accounting principles in the United States of America, or U.S. GAAP. Any reference in these notes to applicable guidance is meant to refer to the authoritative U.S. GAAP as found in the Accounting Standards Codification, or ASC, and Accounting Standards Update, or ASU, of the Financial Accounting Standards Board, or FASB.

**C4 Therapeutics, Inc.****Notes to Consolidated Financial Statements — Continued*****Principles of consolidation***

The Company's consolidated financial statements include the accounts of C4 Therapeutics, Inc. and its wholly owned subsidiary, C4T Securities Corporation, a Massachusetts securities corporation. All significant intercompany balances and transactions have been eliminated in consolidation.

***Use of estimates***

The preparation of consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities as of the date of the consolidated financial statements and the reported amounts of revenues and expenses during the reporting period. The Company bases its estimates and assumptions on historical experience when available and on various factors that it believes to be reasonable under the circumstances. This process may result in actual results differing materially from those estimated amounts used in the preparation of the consolidated financial statements if these results differ from historical experience or other assumptions do not turn out to be substantially accurate, even if such assumptions are reasonable when made. Significant estimates and assumptions reflected in these consolidated financial statements include, but are not limited to, amounts and timing of revenues recognized under the Company's research and development collaboration arrangements, prepaid and accrued research and development expense, incremental borrowing rate used in the measurement of lease liability, and estimated volatility used in our valuation of stock-based awards. The Company assesses estimates on an ongoing basis; however, actual results could materially differ from those estimates.

***Segments***

Operating segments are defined as components of an enterprise for which separate and discrete information is available for evaluation by the chief operating decision-maker in deciding how to allocate resources and assess performance. The Company has one operating segment. The Company's chief operating decision maker, its Chief Executive Officer, manages the Company's operations on a consolidated basis for the purpose of allocating resources. All of the Company's long-lived assets are held in the United States.

***Cash equivalents***

The Company considers all highly liquid investments with a maturity of three months or less when purchased to be cash equivalents. The Company's cash equivalents are measured at fair value on a recurring basis.

***Marketable securities***

The Company classifies marketable securities with a remaining maturity when purchased of greater than three months as available-for-sale. Marketable securities with a remaining maturity date greater than one year are classified as non-current assets. Available-for-sale securities are carried at fair value with the unrealized gains and losses included in accumulated other comprehensive (loss) income as a component of stockholders' equity until realized. Any premium or discount arising at purchase is amortized and/or accreted to interest income and/or expense over the life of the instrument. Realized gains and losses are determined using the specific identification method and are included in other income (expense).

***Restricted cash***

Restricted cash consists of cash placed in a separate restricted bank account as required under the terms of the Company's lease agreements for its Watertown, Massachusetts facilities, as further described within Note 6, *Leases*.

***Concentrations of credit risk***

Financial instruments that potentially subject the Company to significant concentration of credit risk consist primarily of cash, cash equivalents, marketable securities, and restricted cash. The Company may maintain deposits in financial institutions in excess of government insured limits. The Company believes that it is not exposed to significant credit risk as its deposits are held at financial institutions that management believes to be of high credit quality and the Company has not experienced any losses on these deposits. Additionally, the Company has established guidelines relative to credit ratings and maturities intended to safeguard principal balances and maintain liquidity. The Company maintains its funds in accordance with its investment policy, which defines allowable investments, specifies credit quality standards and is designed to limit credit exposure to any single issuer.

***Fair value of financial instruments***

ASC Topic 820, *Fair Value Measurement*, or ASC 820, establishes a fair value hierarchy for instruments measured at fair value that distinguishes between assumptions based on market data (observable inputs) and the Company's own

**C4 Therapeutics, Inc.****Notes to Consolidated Financial Statements — Continued**

assumptions (unobservable inputs). Observable inputs are those that market participants would use in pricing the asset or liability based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumptions about the inputs that market participants would use in pricing the asset or liability and are developed based on the best information available in the circumstances. ASC 820 identifies fair value as the exchange price or exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As a basis for considering market participant assumptions in fair value measurements, ASC 820 establishes a three-tier value hierarchy that distinguishes between the following:

- Level 1—Quoted market prices in active markets for identical assets or liabilities.
- Level 2—Inputs other than Level 1 inputs that are either directly or indirectly observable, such as quoted market prices, interest rates and yield curves.
- Level 3—Unobservable inputs developed using estimates of assumptions developed by the Company, which reflect those that a market participant would use.

To the extent the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair values requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized as Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement. The Company evaluates transfers between levels at the end of each reporting period.

***Property and equipment***

Property and equipment are recorded at cost. Expenditures for repairs and maintenance are expensed as incurred. When assets are retired or disposed of, the assets and related accumulated depreciation are derecognized from the accounts, and any resulting gain or loss is included in the determination of net loss.

Depreciation on equipment is calculated using the straight-line method over the estimated useful lives of the assets as follows:

<b>Asset category</b>	<b>Estimated useful life</b>
Laboratory equipment	5 years
Computer equipment	3 years
Office equipment, furniture and fixtures	5 years
Leasehold improvements	Lesser of useful life or remaining lease term

***Leases***

The Company accounts for leases in accordance with ASC Topic 842, *Leases*, or ASC 842. At the inception of an arrangement, the Company determines whether the arrangement is or contains a lease based on specific facts and circumstances present, the existence of an identified asset(s), if any, and the Company's control over the use of the identified asset(s), if applicable. As provided by ASC 842, the Company elected to combine lease and non-lease components as a single component for all leases. Operating lease liabilities and their corresponding right-of-use assets are recorded based on the present value of future lease payments over the expected lease term. Certain adjustments to the right-of-use asset may be required for items such as incentives received. The Company typically only includes an initial lease term in its assessment of a lease arrangement; options to renew a lease are not included in the assessment unless there is reasonable certainty that the Company will renew. The interest rate implicit in lease contracts is typically not readily determinable. As such, in calculating the lease liability, the Company utilizes its incremental borrowing rate, which is the rate incurred to borrow on a collateralized basis over a similar term an amount equal to the lease payments in a similar economic environment. Lease expense is recognized over the expected lease term on a straight-line basis.

***Impairment of long-lived assets***

The Company evaluates its long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability of assets to be held and used is measured by a comparison of the carrying amount of an asset to future undiscounted net cash flows expected to be generated by the asset. If such assets are considered to be impaired, the impairment to be recognized is measured by the amount by which the carrying amount of the assets exceed the fair value of the assets. Assets to be disposed of are reported at the lower of the carrying amount or fair value less costs to sell.

***Commitments and contingencies***

Liabilities for loss contingencies arising from claims, assessments, litigation, fines and penalties and other sources are recorded when it is probable that a liability has been incurred and the amount can be reasonably estimated. Legal costs incurred in connection with loss contingencies are expensed as incurred.

***Revenue recognition***

The Company recognizes revenue in accordance with ASC Topic 606, *Revenue from Contracts with Customers*, or ASC 606. This standard applies to all contracts with customers, except for contracts that are within the scope of other standards. Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services.

The Company enters into collaboration and licensing agreements with strategic partners, which are within the scope of ASC 606, under which it may exclusively license rights to research, develop, manufacture, and commercialize its product candidates to third parties. The terms of these arrangements typically include payment to the Company of one or more of the following: (1) non-refundable, upfront license fees; (2) reimbursement of certain costs; (3) customer option fees for additional goods or services; (4) development milestone payments; (5) regulatory and commercial milestone payments; and (6) royalties on net sales of licensed products.

In determining the appropriate amount of revenue to be recognized as it fulfills its obligations under each of its agreements, the Company performs the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) the Company satisfies each performance obligation. As part of the accounting for these arrangements, the Company must use its judgment to determine: (a) the number of performance obligations based on the determination under step (ii) above; (b) the transaction price under step (iii) above; (c) the stand-alone selling price for each performance obligation identified in the contract for the allocation of transaction price in step (iv) above; and (d) the contract term and pattern of satisfaction of the performance obligations under step (v) above. The Company uses judgment to determine whether milestones or other variable consideration, except for royalties, should be included in the transaction price as described further below. The transaction price is 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.

Amounts due to the Company for satisfying the revenue recognition criteria or that are contractually due based upon the terms of the collaboration agreements are recorded as accounts receivable in the Company's consolidated balance sheet. Amounts received prior to satisfying the revenue recognition criteria are recorded as deferred revenue in the Company's consolidated balance sheets. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as current deferred revenue. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, net of current portion.

***Upfront license fees***

If the license to the Company's intellectual property is determined to be distinct from the other promises or performance obligations identified in the arrangement, the Company recognizes revenue from non-refundable, upfront fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. In assessing whether a promise or performance obligation is distinct from the other promises, the Company considers factors such as the research, manufacturing, and commercialization capabilities of the customer; the retention of any key rights by the Company; and the availability of the associated expertise in the general marketplace. In addition, the Company considers whether the customer can benefit from a promise for its intended purpose without the receipt of the remaining promises, whether the value of the promise is dependent on the unsatisfied promise, whether there are other vendors that could provide the remaining promise and whether it is separately identifiable from the remaining promise. For licenses that are combined with other promises, the Company exercises 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.

**C4 Therapeutics, Inc.****Notes to Consolidated Financial Statements — Continued***Customer options*

If an arrangement is determined to contain customer options that allow the customer to acquire additional goods or services, the goods and services underlying the customer options are not considered to be performance obligations at the outset of the arrangement, as they are contingent upon option exercise. The Company evaluates the customer options for material rights or options to acquire additional goods or services for free or at a discount. If the customer options are determined to represent a material right, the material right is recognized as a separate performance obligation at the outset of the arrangement. The Company allocates the transaction price to material rights based on the relative standalone selling price, which is determined based on the identified discount and the probability that the customer will exercise the option. Amounts allocated to a material right are not recognized as revenue until, at the earliest, the option is exercised. If an option is not exercised and the target is terminated, the Company will accelerate and recognize all remaining revenue related to the material right performance obligation.

*Research and development services*

The promises under the Company's collaboration agreements may include research and development services to be performed by the Company for or on behalf of the customer. Payments or reimbursements resulting from the Company's research and development efforts are recognized as the services are performed and presented on a gross basis because the Company is the principal for such efforts. Reimbursements from and payments to the customer that are the result of a collaborative relationship with the customer, instead of a customer relationship, such as co-development activities, are recorded as a reduction to research and development expense.

*Milestone payments*

At the inception of each arrangement that includes development milestone payments, the Company evaluates whether the milestones are considered probable of being achieved and estimates the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of the Company or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. The Company evaluates factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the particular milestone in making this assessment. There is considerable judgment involved in determining whether it is probable that a significant revenue reversal would not occur. At the end of each subsequent reporting period, the Company reevaluates the probability of achievement of all milestones subject to constraint and, if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment.

For further discussion of accounting for collaboration revenues, see *Note 8. Collaboration and license agreements*.

***Research and development***

Research and development costs are expensed as incurred. Research and development costs include salaries, stock-based compensation and other employee benefit expenses, lab related supplies and other operational costs related to the Company's research and development activities, including allocated facility-related expenses and external costs of outside vendors engaged to conduct research and development activities. Costs associated with licenses of technology are expensed as incurred and are included in research and development expense in the consolidated statement of operations and comprehensive loss. As part of the process of preparing the consolidated financial statements, the Company is required to estimate their accrued research and development expenses. The Company makes estimates of the accrued expenses as of each balance sheet date in the consolidated financial statements based on facts and circumstances known at that time. In addition, there may be instances in which payments made to the Company's vendors will exceed the level of services provided and result in a prepayment of the expense in which case such amounts are reflected as prepaid expenses and other current assets. In accruing service fees, the Company estimates the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the estimate, the Company adjusts the accrual or the amount of prepaid expenses accordingly. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized in prepaid expenses and other current assets. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

***Stock-based compensation***

The Company measures and recognizes stock-based compensation expense based on the grant date fair value of equity awards measured using the Black-Scholes option pricing model. The Black-Scholes option pricing model estimates the fair

**C4 Therapeutics, Inc.****Notes to Consolidated Financial Statements — Continued**

value of the equity award using the expected term, expected volatility, risk-free interest rate, dividend rate, and the fair value of the common stock underlying the stock-based award.

- The Company estimates the expected term using the “simplified” method, whereby, the expected term equals the arithmetic average of the vesting term and the contractual term of the option.
- Due to the lack of sufficient company-specific historical and implied volatility data, the Company has based its computation of expected volatility on the historical volatility of a representative group of public companies with similar characteristics to the Company, including stage of product development and life science industry focus.
- The risk-free interest rates for periods within the expected life of the option were based on the U.S. Treasury yield curve in effect during the period the options were granted.
- The expected dividend yield is assumed to be zero as the Company has never paid dividends and currently has no plans to pay any dividends on its common stock.
- The fair value of the common stock underlying shared based awards is the quoted market price of the Company’s common stock on the date of the grant.
- The Company recognizes forfeitures as they occur.

The fair value of the awards are recognized as stock-based compensation expense on a straight-line basis over the requisite service period of the awards, which is generally the vesting period. For awards subject to both performance and service-based vesting conditions, we recognize stock-based compensation expense over the remaining service period if the performance condition is considered probable of achievement using management’s best estimates. Stock-based compensation expense is classified in the consolidated statement of operations and comprehensive loss in the same manner in which the award recipients’ payroll costs are classified or in which the award recipients’ service payments are classified.

***Income taxes***

The Company accounts for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequence of events that have been recognized in the consolidated financial statements or the Company’s tax returns. Under this method, deferred tax assets and liabilities are determined based on 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. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes. The Company assesses the likelihood that its deferred tax assets will be recovered from future taxable income and, to the extent it believes, based upon the weight of available evidence, that it is more likely than not that all or a portion of the deferred tax assets will not be realized, a valuation allowance is established.

The Company accounts for uncertain tax positions recognized in the consolidated financial statements by prescribing a more-likely-than-not threshold for financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. The provision for income taxes includes the effects of any resulting tax reserves, or unrecognized tax benefits, which are considered appropriate as well as the related net interest and penalties.

***Comprehensive loss***

Comprehensive loss is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources. Comprehensive loss includes net loss as well as other changes in stockholders’ equity which includes certain changes in equity that are excluded from net loss. The Company’s only element of other comprehensive income is unrealized gains and losses on marketable securities.

***Net loss per share***

Basic net loss per share and diluted net loss per share are computed using the weighted-average number of shares of common stock outstanding for the period. The Company computes diluted (loss) earnings per share after giving consideration to the dilutive effect of stock options and unvested restricted stock that are outstanding during the period, except where such securities would be anti-dilutive.

Common stock equivalent shares are excluded from the computation of diluted net loss per share if their effect is antidilutive. In periods in which the Company reports a net loss, diluted net loss per share is generally the same as basic net loss per share since dilutive common shares are not assumed to have been issued if their effect is anti-dilutive.



## C4 Therapeutics, Inc.

## Notes to Consolidated Financial Statements — Continued

**Going concern**

At each reporting period, the Company evaluates whether there are conditions or events that raise substantial doubt about the Company's ability to continue as a going concern within one year after the date that the consolidated financial statements are issued. The Company is required to make certain additional disclosures if it concludes substantial doubt exists and it is not alleviated by the Company's plans or when its plans alleviate substantial doubt about the Company's ability to continue as a going concern. The Company's evaluation entails analyzing prospective operating budgets and forecasts for expectations of the Company's cash needs and comparing those needs to the current cash, cash equivalent, and marketable securities balances.

**Recently adopted accounting standards***Reference rate reform*

In March 2020, the FASB issued ASU 2020-04, *Reference Rate Reform (Topic 848): Facilitation of the Effects of Reference Rate Reform on Financial Reporting*, which provides temporary optional guidance for a limited time to ease the potential accounting impacts associated with transitioning away from reference rates that are expected to be discontinued, such as the London Interbank Offered Rate, or LIBOR.

In January 2021, the FASB also issued ASU 2021-01, *Reference Rate Reform (Topic 848): Scope*, which extends some of Topic 848's optional expedients to derivative contracts modified as a result of rate reform, including certain derivatives that do not reference LIBOR or other reference rates that are expected to be discontinued. The amendments in this ASU affect the guidance in ASU 2020-04 and are effective in the same timeframe as ASU 2020-04. The adoptions of ASU 2020-04 and ASU 2021-01 did not have a material effect on the Company's consolidated financial statements.

In December 2022, the FASB issued ASU 2022-06, *Reference Rate Reform (Topic 848): Deferral of the Sunset Date of Topic 848*, which extends the sunset date of Topic 848 from December 31, 2022, to December 31, 2024, after which entities will no longer be permitted to apply the optional expedients in Topic 848. The adoption of ASU 2022-06, which was effective upon issuance, did not have a material effect on the Company's consolidated financial statements.

*Government assistance*

In November 2021, the FASB issued ASU No. 2021-10, *Government Assistance (Topic 832): Disclosures by Business Entities about Government Assistance*, which requires business entities to provide certain disclosures when they (i) have received government assistance and (ii) use a grant or contribution accounting model by analogy to other accounting guidance. The Company adopted ASU 2021-10 on January 1, 2022 and will apply it to any government assistance received thereafter. The adoption did not have a material effect on the Company's consolidated financial statements.

**Note 3. Fair value measurements**

The following tables present information about the Company's financial assets measured at fair value on a recurring basis and indicates the level of the fair value hierarchy utilized to determine such fair values as of December 31, 2022 (in thousands):

	Fair Value	Level 1	Level 2	Level 3
<b>Cash equivalents:</b>				
Money market funds	\$ 28,705	\$ 28,705	\$ —	\$ —
U.S. Treasury securities	799	—	799	—
<b>Marketable securities:</b>				
Corporate debt securities	234,327	—	234,327	—
U.S. government debt securities	47,641	—	47,641	—
U.S. Treasury securities	25,393	—	25,393	—
<b>Total cash equivalents and marketable securities</b>	<b>\$ 336,865</b>	<b>\$ 28,705</b>	<b>\$ 308,160</b>	<b>\$ —</b>

**C4 Therapeutics, Inc.**
**Notes to Consolidated Financial Statements — Continued**

The following table sets forth the fair value of the Company's financial assets by level within the fair value hierarchy at December 31, 2021 (in thousands):

	Fair Value	Level 1	Level 2	Level 3
<b>Cash equivalents:</b>				
Money market funds	\$ 59,162	\$ 59,162	\$ —	\$ —
Corporate debt securities	11,649	—	11,649	—
U.S. Treasury securities	5,000	—	5,000	—
<b>Marketable securities:</b>				
Corporate debt securities	308,300	—	308,300	—
U.S. government debt securities	37,883	—	37,883	—
U.S. Treasury securities	29,172	—	29,172	—
<b>Total cash equivalents and marketable securities</b>	<b>\$ 451,166</b>	<b>\$ 59,162</b>	<b>\$ 392,004</b>	<b>\$ —</b>

The Company classifies its money market funds, which are valued based on quoted market prices in active markets, with no valuation adjustment, as Level 1 assets within the fair value hierarchy.

Marketable securities consist of U.S. Treasury securities, U.S. government debt securities, and corporate debt securities, all of which are classified as available-for-sale pursuant to ASC 320, *Investments – Debt and Equity Securities*. Marketable securities are classified within Level 2 of the fair value hierarchy because pricing inputs are other than quoted prices in active markets, which are either directly or indirectly observable as of the reporting date, and fair value is determined using models or other valuation methodologies on a recurring basis.

**Note 4. Marketable securities**

Marketable securities at December 31, 2022 consisted of the following (in thousands):

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
<b>Marketable securities, current:</b>				
Corporate debt securities	\$ 183,270	\$ 2	\$ (2,068)	\$ 181,204
U.S. government debt securities	40,986	—	(1,184)	39,802
U.S. Treasury securities	25,650	—	(257)	25,393
<b>Marketable securities, non-current</b>				
Corporate debt securities	53,592	2	(471)	53,123
U.S. government debt securities	8,000	—	(161)	7,839
<b>Total marketable securities, current and non-current</b>	<b>\$ 311,498</b>	<b>\$ 4</b>	<b>\$ (4,141)</b>	<b>\$ 307,361</b>

Marketable securities at December 31, 2021 consisted of the following (in thousands):

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
<b>Marketable securities, current:</b>				
Corporate debt securities	\$ 219,414	\$ 1	\$ (250)	\$ 219,165
U.S. government debt securities	8,987	—	(3)	8,984
U.S. Treasury securities	5,006	—	—	5,006
<b>Marketable securities, non-current</b>				
Corporate debt securities	89,538	—	(403)	89,135
U.S. government debt securities	32,982	—	(105)	32,877
U.S. Treasury securities	20,203	—	(15)	20,188
<b>Total marketable securities, current and non-current</b>	<b>\$ 376,130</b>	<b>\$ 1</b>	<b>\$ (776)</b>	<b>\$ 375,355</b>

## C4 Therapeutics, Inc.

## Notes to Consolidated Financial Statements — Continued

Marketable securities classified as current have maturities of less than one year. Marketable securities classified as non-current are those that: (i) have a maturity of greater than one year, and (ii) we do not intend to liquidate within the next twelve months, although these funds are available for use and, therefore, are classified as available-for-sale. No available-for-sale debt securities held as of December 31, 2022 or December 31, 2021 had remaining maturities greater than five years.

Marketable securities in unrealized loss positions as of December 31, 2022 consisted of the following (in thousands, except number of securities):

	Number of Securities	Fair Value	Gross Unrealized Losses
Marketable securities in continuous unrealized loss position for less than 12 months:			
Corporate debt securities	63	\$ 134,027	\$ (1,262)
U.S. government debt securities	6	15,748	(245)
U.S. Treasury securities	4	5,575	(11)
Marketable securities in continuous unrealized loss position for greater than 12 months:			
Corporate debt securities	36	82,375	(1,277)
U.S. government debt securities	7	31,892	(1,100)
U.S. Treasury securities	4	19,817	(246)
Total marketable securities in unrealized loss position	<u>120</u>	<u>\$ 289,434</u>	<u>\$ (4,141)</u>

Marketable securities in unrealized loss positions as of December 31, 2021 consisted of the following (in thousands, except number of securities):

	Number of Securities	Fair Value	Gross Unrealized Losses
Marketable securities in continuous unrealized loss position for less than 12 months:			
Corporate debt securities	110	\$ 303,450	\$ (653)
U.S. government debt securities	8	37,883	(108)
U.S. Treasury securities	5	24,172	(15)
Total marketable securities in unrealized loss position	<u>123</u>	<u>\$ 365,505</u>	<u>\$ (776)</u>

As of December 31, 2021, no marketable securities were in a continuous unrealized loss position for 12 months or longer.

Based on factors such as historical experience, market data, issuer-specific factors, and current economic conditions, the Company did not record an allowance for credit losses at December 31, 2022 and December 31, 2021, related to these securities.

## C4 Therapeutics, Inc.

## Notes to Consolidated Financial Statements — Continued

**Note 5. Property and equipment**

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

	As of December 31,	
	2022	2021
Property and equipment		
Laboratory equipment	\$ 8,757	\$ 8,276
Leasehold improvements	4,682	541
Furniture and fixtures	1,181	805
Office equipment	529	179
Computer equipment	191	223
Construction in progress	183	—
Total property and equipment	15,523	10,024
Less: accumulated depreciation	(8,123)	(6,916)
Total property and equipment, net	\$ 7,400	\$ 3,108

Depreciation expense related to property and equipment was as follows (in thousands):

	Years Ended December 31,	
	2022	2021
Depreciation expense	\$ 1,676	\$ 1,492

**Note 6. Leases**

In July 2017, the Company entered into a lease of office and laboratory space for its headquarters in Watertown, Massachusetts, or the Watertown Lease. The Watertown Lease had a non-cancelable term of ten years with an option to extend for one additional five-year period and is subject to rent escalation throughout the term. Additionally, the Watertown Lease required the Company to provide collateral, which was recorded as restricted cash on the consolidated balance sheets. The Watertown Lease commenced in April 2018. The Watertown Lease was classified as an operating lease and, upon the commencement in April 2018, the Company recorded a lease liability of \$15.1 million and a right-of-use asset of \$16.7 million, which is inclusive of \$1.5 million of construction costs funded by the Company. In initially calculating the lease liability and the right-of-use asset, the Company did not include the additional five-year period option as management did not believe there was reasonable certainty that the Company would exercise the option. In addition to rent, the Company is also responsible for paying its pro rata share of costs incurred for common area maintenance, real estate taxes and property insurance related to the leased space, which are accounted for as variable lease costs.

In November 2021, the Company entered into an amendment to the Watertown Lease, or the Amended Lease. The Amended Lease serves to extend the lease term of the Company's existing leased space, or the Existing Leased Space, and provides additional office and laboratory space, or the Newly Leased Space. The Amended Lease commenced in January 2022 and the Company's obligation to pay rent on the Newly Leased Space commenced in March 2022, with the amount of this new rent obligation added to the Company's continuing obligation to pay rent on the Existing Leased Space. The Amended Lease terminates in March 2032, which is 10 years from the rent commencement date for the Newly Leased Space. The Amended Lease is subject to fixed rate rent escalations, provides for up to \$2.6 million in tenant improvements, and provides an option for the Company to extend the lease term of the Amended Lease for one additional five-year period. Upon executing the Amended Lease, the Company increased its collateral to \$3.3 million, which is recorded as restricted cash on the accompanying consolidated balance sheets as of December 31, 2022 and 2021. In addition to rent, under the terms of the Amended Lease, the Company is also responsible for paying its pro rata share of costs incurred for common area maintenance, real estate taxes and property insurance related to the leased space, including both the Existing Leased Space and, as of January 2022, the Newly Leased Space, which amounts are accounted for as variable lease costs.

*Accounting for the amended lease*

As the Amended Lease extends the term of the Existing Leased Space and provides access to the Newly Leased Space, in accordance with the provisions of ASC 842, the Company accounted for the Amended Lease as two separate contracts: 1) modification of the existing lease agreement to extend the lease term of the Existing Leased Space, and 2) new lease agreement for the right-of-use of the Newly Leased Space.

## C4 Therapeutics, Inc.

## Notes to Consolidated Financial Statements — Continued

As the Company maintained control of the Existing Leased Space upon execution of the Amended Lease, the Company recorded an increase in right-of-use asset and lease liability of \$20.1 million related to the new rental payments during the extended term and current incremental borrowing rate of the Existing Leased Space upon execution of the Amended Lease. The calculation of the lease liability and the right-of-use asset of the Existing Leased Space does not include the additional five-year period option as the Company does not believe there is reasonable certainty that the option will be exercised.

As noted above, the lease for the Newly Leased Space commenced in January 2022. As a result, the Company recorded a right-of-use asset of \$44.4 million, and a corresponding lease liability of \$44.1 million for the Newly Leased Space. The calculation of the lease liability and the right-of-use asset of the Newly Leased Space does not include the additional five-year period option provided under the Amended Lease as the Company does not believe there is reasonable certainty that the option will be exercised. As stated above, the Amended Lease provides for up to \$2.6 million of tenant improvement allowance. As of December 31, 2022, the Company has used the full \$2.6 million of tenant improvement allowance.

In May 2022, the Company entered into a sublease agreement with a third party, or the Sublease, for a portion of the office and laboratory space in Suite 200 at 490 Arsenal Way, Watertown, Massachusetts. The term of the Sublease ends in June 2025.

The elements of lease costs were as follows (in thousands):

	Years Ended December 31,	
	2022	2021
Lease cost:		
Operating lease cost	\$ 10,031	\$ 2,686
Variable lease cost	2,026	857
Sublease income	(1,481)	—
Total lease cost	\$ 10,576	\$ 3,543

The following table summarizes the lease term and incremental borrowing rate applied in arriving at the lease liability:

	As of December 31,	
	2022	2021
Remaining lease term	9.1 years	10.2 years
Incremental borrowing rate	5.3 %	5.2 %

Future lease payments under non-cancelable leases as of December 31, 2022 for each of the years ending December 31 are as follows (in thousands):

Undiscounted lease payments:	
2023	\$ 8,571
2024	8,828
2025	9,093
2026	9,366
2027	9,646
Thereafter	52,113
Total undiscounted lease payments	97,617
Less: imputed interest	(21,947)
Total operating lease liability as of December 31, 2022	\$ 75,670

## C4 Therapeutics, Inc.

## Notes to Consolidated Financial Statements — Continued

**Note 7. Accrued expenses and other current liabilities**

Accrued expenses and other current liabilities consisted of the following (in thousands):

	As of December 31,	
	2022	2021
Accrued expenses and other current liabilities:		
Accrued research and development	\$ 9,824	\$ 6,863
Accrued compensation and benefits	6,831	5,084
Accrued professional fees	1,062	1,246
Other	2,052	413
Total accrued expenses and other current liabilities	<u>\$ 19,769</u>	<u>\$ 13,606</u>

**Note 8. Collaboration and license agreements*****Roche Collaboration and License Agreement***

In March 2016, the Company entered into a license agreement with Roche, which was amended in June 2016 and amended further in March 2017. The Company and Roche amended and restated that agreement (as so amended) in December 2018. This amended and restated agreement is referred to as the Roche Agreement. Under the Roche Agreement, the Company and Roche agreed to collaborate in the research, development, manufacture and commercialization of target-binding degrader medicines using the Company's proprietary TORPEDO platform for the treatment of cancers and other indications. Under the Roche Agreement, the Company may elect to opt into certain co-development rights, in which case the Company will receive an increased royalty rate on future product sales from products directed to that target. In addition, if the Company opts into certain co-detailing rights, it is also entitled to reimbursement of certain commercialization costs. Upon entry into the Roche Agreement, the Company received additional upfront consideration of \$40.0 million from Roche.

In November 2020, the Company signed a further amendment, the effect of which was to provide that the parties would develop up to five potential targets, with Roche maintaining its option rights to license and commercialize products directed to those targets. The November 2020 amendment also provides a mechanism through which the Company and Roche can mutually agree to terminate the Roche Agreement on a target-by-target basis by the entry into a Mutual Target Termination Agreement. Upon the entry into a Mutual Target Termination Agreement, the Roche Agreement provides that all rights and responsibilities for know-how and other intellectual property in support of products that use inhibition as their mode of action revert to Roche and all rights and responsibilities for know-how and other intellectual property in support of products that use degradation as their mode of action revert to the Company. In support of this allocation of rights, Roche provides the Company, and the Company provides Roche, with a perpetual irrevocable, fully paid up, exclusive (even as to party granting the license), sublicensable (including in multiple tiers) license to the patents and know-how that are allocated to a party under a Mutual Target Termination Agreement. As the research activities with Roche have progressed and evolved over time, there are now three targets on which the parties continue to collaborate, with Roche maintaining its option rights to license and commercialize products directed to those three targets.

Under the Roche Agreement, the Company receives annual research plan payments of \$1.0 million for up to three years for each active research plan. For certain targets, Roche is required to pay the Company fees of \$2.0 million and \$3.0 million upon the progression of targets to the lead series identification achievement and good laboratory practice toxicology study phase, respectively. Finally, adjustments were made to the option exercise fees, whereby targets that have progressed through standard good laboratory practice, or GLP, toxicology studies at the time of exercise now have option exercise fees of \$7.0 million to \$12.0 million and those progressed through Phase 1 trials have option exercise fees of \$20.0 million. For each target option exercised by Roche, the Company is eligible to receive milestone payments ranging from \$260.0 million to \$275.0 million upon the achievement of certain development and commercial milestones with respect to corresponding products, subject to certain reductions and exclusions based on intellectual property coverage. Roche is also required to pay the Company up to \$150.0 million per target in one-time sales-based milestone payments upon the achievement of specified levels of net sales of a product directed to such target. Finally, Roche is required to pay the Company tiered royalties ranging from the mid-single digits to mid-teen percentages on net sales of products sold by Roche pursuant to its exercise of its option rights, subject to certain reductions. For sales of products for which the Company exercises its co-development right, the applicable royalty rates will be increased by a low-single digit percentage.

## C4 Therapeutics, Inc.

## Notes to Consolidated Financial Statements — Continued

The collaboration is managed by a joint research committee. The Company has control over the joint research committee prior to Roche's exercise of its option rights as to a particular target, with Roche assuming control of the joint research committee thereafter, and may terminate the Roche Agreement on a target-by-target or product-by-product basis under several scenarios, upon at least 90 days' prior written notice.

*Roche Agreement accounting*

At commencement, the Company identified twelve performance obligations within the Roche Agreement, represented by the six potential research and development targets then included in the collaboration and the option rights held by Roche for each of those six targets. A non-exclusive royalty-free license to use the Company's intellectual property to conduct research and development activities and participation on joint research committee were identified as promised services. However, the Company determined that the research and development license and research and development services were not distinct from one another, and participation on the joint research committee was determined to be quantitatively and qualitatively immaterial.

The total transaction price of the Roche Agreement is allocated to the performance obligations based on their relative standalone selling price. The allocated transaction price is recognized as revenue from collaboration agreements in one of two ways:

- **Research and development targets:** The Company recognizes the portion of the transaction price allocated to each of the research and development performance obligations as the research and development services are provided, using an input method, in proportion to costs incurred to date for each research development target as compared to total costs incurred and expected to be incurred in the future to satisfy the underlying obligation related to said research and development target. The transfer of control occurs over this period and, in management's judgment, is the best measure of progress towards satisfying the performance obligation.
- **Option rights:** The transaction price allocated to the options rights, which are considered material rights, is recognized in the period that Roche elects to exercise or elects to not exercise its option right to license and commercialize the underlying research and development target.

The following table summarizes the allocation of the total transaction price to the identified performance obligations under the arrangement, and the amount of the transaction price unsatisfied as of December 31, 2022 (in thousands):

	Transaction Price Allocated	Transaction Price Unsatisfied
Performance obligations:		
Research and development targets	\$ 61,074	\$ 25,542
Option rights	6,748	2,502
Total	<u>\$ 67,822</u>	<u>\$ 28,044</u>

Amounts due to the Company that have not yet been received are recorded as accounts receivable and amounts received that have not yet been recognized as revenue are recorded as deferred revenue on the Company's consolidated balance sheet.

***Biogen Collaboration Research and License Agreement***

In December 2018, the Company entered into a collaboration research and license agreement, or the Biogen Agreement, with Biogen. In February 2020, the Company and Biogen amended the Biogen Agreement to provide further clarity around Biogen's ownership of target binding moieties (which are portions of molecules), and any related intellectual property that are directed at or bind to collaboration targets. This amendment further provided that Biogen licenses to the Company rights to use these Biogen target binding moieties and any related intellectual property as needed in order to conduct the research and development activities contemplated under the Biogen Agreement. Pursuant to the terms of the Biogen Agreement, the Company and Biogen agreed to collaborate on research activities to develop novel treatments for neurological conditions such as Alzheimer's disease and Parkinson's disease through medicines that rely on target protein degradation, or TPD, as their mode of action, all of which are created using the Company's degrader technology. Under the terms of the Biogen Agreement, the Company was engaged to develop TPD therapeutics that utilize degrader technology for up to five target proteins over a period of 54 months, ending in June 2023. On a target-by-target basis, after successful completion of a defined target evaluation period, Biogen assumes full rights and responsibility for continued development of each target.

**C4 Therapeutics, Inc.****Notes to Consolidated Financial Statements — Continued**

In exchange for the non-exclusive research license from Biogen, as well as a \$45.0 million nonrefundable upfront payment, the Company has granted a license to develop, commercialize, and manufacture products related to each of the targets (which is contingent on not cancelling the agreement), performs initial research services for drug discovery, has provided a non-exclusive research and commercial license to its intellectual property, and participates on the joint steering committee, or the Biogen JSC. The Company was also obligated to participate in early research activities for other potential targets or sandbox activities, at Biogen's election up to a maximum amount; any work performed for these services is reimbursed by Biogen, and Biogen reimburses the Company for certain FTE costs. The Company's obligations under the sandbox activities were completed as of August 31, 2021. For any target, following the achievement of development candidate criteria and prior to any IND-enabling study, Biogen will bear all costs and expenses of and will have sole discretion and decision-making authority with respect to the performance of further activities with respect to any degrader under development under the Biogen Agreement and all products that incorporate that degrader. Biogen is also required to pay the Company up to \$35.0 million per target in development milestones and \$26.0 million per target in one-time sales-based payments for the first product to achieve certain levels of net sales. In addition, Biogen is required to pay the Company royalties on a licensed product-by-licensed product basis, on worldwide net product sales. All milestone and sales-based payments are made after the Company has met the defined criteria in the joint research plan for that target, at which time Biogen will have control of the products related to the targets for commercialization; the receipt of these payments is contingent on the further development of products directed to the targets to commercialization by Biogen, without any additional research and development efforts from the Company.

The collaboration is managed by the Biogen JSC, which Biogen has control over, and Biogen may terminate the Biogen Agreement on a target-by-target or product-by-product basis under several scenarios, upon at least 90 days' prior written notice.

*Biogen Agreement accounting*

The Company recognizes revenue under the Biogen Agreement from two types of services: 1) research and development services, and 2) sandbox activities, which are discovery-type research services.

- **Research and development services:** The Company identified one performance obligation at the outset of the Biogen Agreement, representing a combined performance obligation consisting of (1) the licenses, (2) the research activities for the target evaluation phase for all five targets and (3) the joint research plan phase for each target. The Company determined that the licenses and research activities were not distinct from one another, as the licenses have limited value without the performance of the research activities by the Company. Participation on the Biogen JSC to oversee the research activities and the technology transfer associated with the Biogen License Agreement were determined to be quantitatively and qualitatively immaterial and therefore are excluded from performance obligations. The Company recognizes the transaction price allocated to this performance obligation as the research and development services are provided, using an input method, in proportion to costs incurred to date for each research development target as compared to total costs incurred and expected to be incurred in the future to satisfy the underlying obligation related to said research and development target. The transfer of control occurs over this period and, in management's judgment, is the best measure of progress towards satisfying the performance obligation.
- **Sandbox activities:** Biogen had the option to fund sandbox activities in exchange for consideration at market rates, whereby the Company would perform discovery-type research at Biogen's election to develop other potential targets that may be used as replacement targets for the initially nominated targets or two additional targets under the Biogen Agreement. Revenues earned under this option were recognized as services were performed and were not included in the transaction price allocated to the performance obligation described above. The Company recognized FTE reimbursement received for sandbox activities as revenue as incurred each quarter. As noted above, sandbox activities fully concluded on August 31, 2021.

As of December 31, 2022, total transaction price of \$55.0 million is allocated to the research and development services performance obligation and \$11.4 million of the allocated transaction price remains unsatisfied. The transaction price as of December 31, 2022 includes \$6.0 million of milestones earned during the year ended December 31, 2021.

Amounts due to the Company that have not yet been received are recorded as accounts receivable and amounts received that have not yet been recognized as revenue are recorded in deferred revenue on the Company's consolidated balance sheet.



***Calico Collaboration and License Agreement***

In March 2017, the Company entered into a collaboration and license agreement, or the Calico Agreement, with Calico whereby the Company and Calico agreed to collaborate to develop and commercialize small molecule protein degraders for diseases of aging, including cancer, for a five-year period ending in March 2022. In August 2021, the Company provided Calico with an option to extend the research term with respect to a certain program for up to a one-year period ending in March 2023. In September 2021, Calico exercised the option resulting in a \$1.0 million extension payment to the Company. In addition, Calico will continue to reimburse the Company for a number of FTEs, depending on the stage of the research, at specified market rates.

Under the terms of the Calico Agreement, the Company was engaged to develop and commercialize small molecule protein degraders for up to five target proteins over the research term. Under the Calico Agreement, the Company is required to perform initial research and development activities for the nominated targets for drug discovery and preclinical development over the applicable research term, with the intent to provide a development candidate for each target to Calico once the agreed-upon research is complete. In addition, the Company provides Calico with a non-exclusive research and commercial license to its intellectual property and will participate on the Calico joint research committee, or the Calico JRC. Once Calico nominates a target and pays the applicable target initiation fee, the Company will commence research and development activities for that target. Calico is obligated to reimburse the Company for its research and development activities for each target at specified levels through the identification of a development candidate, after which time Calico shall assume full responsibility for candidate development and Calico is entitled to pursue commercial development of products related to that target.

Under the Calico Agreement, Calico paid an upfront amount of \$5.0 million and certain annual payments totaling \$5.0 million through June 30, 2020 and pays target initiation fees and reimburses the Company for a number of FTEs, depending on the stage of the research, at specified market rates. For each target, the Company is eligible to receive up to \$132.0 million in potential development and commercial milestone payments, on sales of all products resulting from the collaboration efforts. Calico is also required to pay the Company up to \$65.0 million in one-time sales-based payments for the first product to achieve certain levels of net sales. In addition, Calico is required to pay the Company royalties, at percentages in the mid-single digits, on a licensed product-by-licensed product basis, on worldwide net product sales. All milestone and sales-based payments are made after the Company has met the defined criteria in the joint research plan for that target, at which time Calico will have control of the products related to targets for commercialization; the receipt of these payments by the Company is contingent on the further development of the targets to commercialized products by Calico, without any additional research and development efforts required by us.

The Calico Agreement is managed by the Calico JRC. Calico has control over the Calico JRC and may terminate the Calico Agreement on a target-by-target or product-by-product basis under several scenarios, upon prior written notice.

In August 2021, the Company provided Calico with an option to extend the research term with respect to a certain program for up to a one-year period ending in March 2023. In September 2021, Calico exercised the option resulting in a \$1.0 million extension payment to the Company. In addition, Calico will continue to reimburse the Company for a number of FTEs, depending on the stage of the research, at specified market rates.

***Calico Agreement accounting***

The Company identified one performance obligation at the outset of the Calico Agreement, which consists of: (1) the non-exclusive license and (2) the research activities for the target evaluation phase for five targets and the joint research plan phase for two targets. The Company determined that the license and research activities were not distinct from one another, as the license has limited value without the performance of the research activities by the Company.

The transaction price consists of the upfront amount, the committed anniversary payments, the target initiation fees related to the targets nominated at the execution of the Calico Agreement, and the extension payment upon exercise of the extension option discussed above. Initially, the Company amortized the transaction price on a straight-line basis over the initial five-year term of the Calico Agreement. Beginning in September 2021, as a result of the extension of the research term for one program and Calico's obligation to pay an additional \$1.0 million in transaction price, the Company now amortizes the revised transaction price on a straight-line basis over the six-year term of the Calico Agreement. Straight-line amortization of the transaction price was considered the best measure of progress because the customer has access to research and development services throughout the period. Incremental fees for research and development services are paid at agreed upon FTE rates and recognized in the period incurred.

**C4 Therapeutics, Inc.**
**Notes to Consolidated Financial Statements — Continued**

As of December 31, 2022, total transaction price of \$13.0 million is allocated to the research and development services performance obligation and \$0.5 million of the allocated transaction price remains unsatisfied.

Amounts due to the Company that have not yet been received are recorded as accounts receivable and amounts received that have not yet been recognized as revenue are recorded in deferred revenue on the Company's consolidated balance sheet.

**Summary of revenue recognized from collaboration agreements**

Revenue from collaboration agreements was as follows (in thousands):

	Years Ended December 31,	
	2022	2021
Revenue from collaboration agreements:		
Roche Agreement	\$ 4,939	\$ 19,379
Biogen Agreement	19,214	15,720
Calico Agreement	6,943	10,686
<b>Total revenue from collaboration agreements</b>	<b>\$ 31,096</b>	<b>\$ 45,785</b>

Supplemental information related to the collaboration and license agreements consisted of the following in the Company's consolidated balance sheet as of December 31, 2022 (in thousands):

	Accounts Receivable	Deferred Revenue, Current	Deferred Revenue, Net of Current	Deferred Revenue, Total
Supplemental information:				
Roche Agreement	\$ 417	\$ 4,649	\$ 16,895	\$ 21,544
Biogen Agreement	—	11,427	—	11,427
Calico Agreement	1,056	542	—	542
<b>Total</b>	<b>\$ 1,473</b>	<b>\$ 16,618</b>	<b>\$ 16,895</b>	<b>\$ 33,513</b>

Supplemental information related to the collaboration and license agreements consisted of the following in the Company's consolidated balance sheet as of December 31, 2021 (in thousands):

	Accounts Receivable	Deferred Revenue, Current	Deferred Revenue, Net of Current	Deferred Revenue, Total
Supplemental information:				
Roche Agreement	\$ 1,215	\$ 5,601	\$ 17,215	\$ 22,816
Biogen Agreement	3,000	24,032	6,611	30,643
Calico Agreement	1,501	2,167	542	2,709
<b>Total</b>	<b>\$ 5,716</b>	<b>\$ 31,800</b>	<b>\$ 24,368</b>	<b>\$ 56,168</b>

Supplemental financial information related to the collaboration and license agreements are (in thousands):

	Years Ended December 31,	
	2022	2021
Revenue recognized that was included in the contract liability at the beginning of the period	\$ 25,412	\$ 34,363
Revenue recognized from performance obligations fully or partially satisfied in previous periods	518	1,654

As of December 31, 2022, the aggregate amount of the transaction price allocated to performance obligations under the Roche Agreement, the Biogen Agreement, and the Calico Agreement that are partially unsatisfied was \$40.0 million.

## C4 Therapeutics, Inc.

## Notes to Consolidated Financial Statements — Continued

**Note 9. Long-term debt and warrant – related party**

On June 5, 2020, contemporaneously with the completion of its Series B Financing the Company entered into a Credit Agreement, or the Credit Agreement, with Perceptive Credit Holdings III, LP, an affiliate of Perceptive Advisors LLC, or Perceptive, that provided for an aggregate principal borrowing amount of up to \$20.0 million, available in two tranches of \$12.5 million and \$7.5 million. Perceptive was considered a related party to the Company based on its ownership of the Company's common stock at inception of the Credit Agreement.

In June 2020, the Company drew down on the first tranche of \$12.5 million, or the Term Loan, which is outstanding as of December 31, 2022. The Company elected not to draw down the second tranche, which expired on June 30, 2021. The Term Loan bears interest at a variable rate using the greater of LIBOR or 1.75%, plus 9.50%. The interest rate was 13.63% as of December 31, 2022, and the Term Loan is secured by a lien on substantially all of the Company's asset. When the LIBOR interest rate is discontinued in the future, it is expected that the interest rate of the Term Loan would switch to Secured Overnight Financing Rate, or SOFR. As of December 31, 2022, the effect of switching from LIBOR to SOFR is not material to the Company's consolidated financial statements.

The Credit Agreement requires the Company to maintain a minimum aggregate cash balance of \$3.0 million in one or more controlled accounts and contains various affirmative and negative covenants that limit its ability to engage in specified types of transactions.

The Company was required to make monthly interest-only payments on the Term Loan through December 5, 2022. In 2023, the Company began to make principal only payments of 2.00% of the Term Loan, plus interest, until June 5, 2024, or the Maturity Date, at which time the outstanding principal and unpaid interest balance is due. If the Company pays off the Term Loan prior to the Maturity Date, it will be required to pay a prepayment fee, which would have been \$1.1 million as of December 31, 2022.

Under the terms of the Credit Agreement, Perceptive held a warrant to purchase up to 338,784 shares of the Company's common stock at an exercise price of \$8.86 per share. As further described in Note 10, *Stockholders' equity*, in May 2021, Perceptive exercised its warrant using the net exercise method provided by the Credit Agreement.

The following table contains the anticipated future minimum payments on long-term debt as of December 31, 2022 for each of the years ending December 31 and a reconciliation to the carrying value of long-term debt on the Company's consolidated balance sheets (in thousands):

Undiscounted, minimum long-term debt payments:	
2023	\$ 3,000
2024	9,500
Total undiscounted, minimum long-term debt payments	12,500
Less: Unamortized debt issuance costs and debt discount	(1,018)
Total long-term debt—related party	<u>\$ 11,482</u>

**Note 10. Stockholders' equity****Common stock**

In October 2020, the Company authorized preferred stock issuable of 10,000,000 shares and increased its authorized common stock issuable to 150,000,000 shares, both with a \$0.0001 par value per share.

The holders of common stock are entitled to one vote for each share held at all meetings of stockholders and written actions in lieu of meetings provided. Subject to full payment of all preferential dividends to which the holders of preferred stock, if any, are entitled, the holders of common stock shall be entitled to receive dividends out of funds legally available. In the event of a liquidation, dissolution, or winding up of the Company, after payment or provision for payment of all debts and liabilities of the Company and all preferential amounts to which the holders of preferred stock, if any, are entitled with respect to the distribution of assets in liquidation, the holders of common stock shall be entitled to share ratably in the remaining assets of the Company available for distribution. The holders of common stock have no preemptive or other subscription rights, and there are no redemption or sinking fund provisions with respect to such stock.

**C4 Therapeutics, Inc.****Notes to Consolidated Financial Statements — Continued***Public offering of common stock*

In June 2021, the Company completed a follow-on public offering, at which time the Company issued 4,887,500 shares of its common stock, including 637,500 shares of common stock that were issued to the underwriters when they exercised in full their overallotment option. Net proceeds from the follow-on public offering, including the exercise in full of the underwriters' option to purchase additional shares, were \$169.5 million, after deducting underwriting discounts and commissions, and expenses.

*Perceptive warrant – related party*

As described in Note 9, *Long-term debt and warrant – related party*, Perceptive held a warrant to purchase up to 338,784 shares of the Company's common stock at an exercise price of \$8.86 per share. In May 2021, Perceptive exercised its warrant using the net exercise method provided by the Credit Agreement. Under the net exercise method, Perceptive requested that the Company withhold the number of shares equivalent to the aggregate exercise price, or \$3.0 million. As a result of the net exercise in May 2021, the Company issued Perceptive 256,038 shares of its common stock.

***At-The-Market Equity Program***

In November 2021, the Company filed an automatically effective registration statement on Form S-3, or the Registration Statement, with the SEC that registers the offering, issuance and sale of an unspecified amount of common stock, preferred stock, debt securities, warrants and/or units of any combination thereof. Simultaneously, the Company entered into an equity distribution agreement with Cowen and Company, LLC, as sales agent, to provide for the issuance and sale by the Company of up to \$200.0 million of common stock from time to time in "at-the-market" offerings under the Registration Statement and related prospectus filed with the Registration Statement, or the ATM Program. For the years ended December 31, 2022 and 2021, no sales have been made under the ATM Program.

**Note 11. Stock-based compensation*****2015 Incentive Stock Option and Grant Plan***

On December 28, 2015, the Company's board of directors adopted the 2015 Incentive Stock Option and Grant Plan, or the 2015 Plan, and reserved 2,525,327 shares of common stock for issuance under this plan.

The 2015 Plan authorized the board of directors or a committee of the board to grant incentive stock options, nonqualified stock options and restricted stock awards to eligible employees, outside directors and consultants of the Company. Options granted under the 2015 Plan generally vest over a period of five or eight years with a cliff vesting at one year and quarterly vesting thereafter and options that lapse or are forfeited are available to be granted again. The contractual life of all options granted under the 2015 Plan is ten years from the date of grant.

***2020 Stock Option and Incentive Plan***

On September 8, 2020, the Company's board of directors adopted the C4 Therapeutics, Inc. 2020 Stock Option and Incentive Plan, or the 2020 Plan, which became effective on September 30, 2020. Upon adoption there were 6,567,144 shares of common stock reserved for issuance under the 2020 Plan. The Company's Board of Directors, the Compensation Committee of the Board of Directors, and, in certain contexts, the Chief Executive Officer of the Company are authorized to grant a broad range of stock-based awards under the 2020 Plan, including stock options, stock appreciation rights, or SARs, restricted stock awards, or RSAs, restricted stock units, or RSUs, performance awards and stock bonus awards to the Company's officers, employees, directors and other key persons, including consultants.

Following the effectiveness of the 2020 Plan, the Company ceased making grants under the 2015 Plan. However, the 2015 Plan continues to govern the terms and conditions of the outstanding awards granted under it. Shares of common stock subject to awards granted under the 2015 Plan that cease to be subject to such awards by forfeiture or otherwise after the termination of the 2015 Plan will be available for issuance under the 2020 Plan. As of December 31, 2022, the Company had an aggregate of 10,972,347 shares reserved under the 2020 Plan and 2015 Plan, of which 3,979,299 shares were available for future issuance under the 2020 Plan.

The 2020 Plan provides for an annual increase, to be added on the first day of each fiscal year, beginning with January 1, 2021 and continuing until the expiration of the 2020 Plan, equal to the lesser of (i) 5% of the outstanding shares of common stock on the immediately preceding December 31st, or (ii) lesser number of shares determined by the administrator of the 2020 Plan, which is the Company's Board of Directors or the Compensation Committee of the Board of Directors. On January 1, 2023, the annual increase for the 2020 Plan resulted in an additional 2,448,310 shares authorized for issuance being added to the 2020 Plan.

**C4 Therapeutics, Inc.**
**Notes to Consolidated Financial Statements — Continued**

Stock-based compensation expense was as follows (in thousands):

	Years Ended December 31,	
	2022	2021
Stock-based compensation expense:		
Research and development	\$ 13,108	\$ 7,526
General and administrative	16,908	13,986
Total stock-based compensation expense	<u>\$ 30,016</u>	<u>\$ 21,512</u>

The following table summarizes the stock option activity under the Company's equity awards plans for the year ended December 31, 2022:

	Number of Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2021	5,983,425	\$ 22.33	8.64	\$ 75,538
Granted	2,296,800	18.93		
Exercised	(181,354)	4.67		
Forfeited/expired	(1,105,819)	23.98		
Outstanding as of December 31, 2022	<u>6,993,052</u>	\$ 21.57	7.78	\$ 1,031
Exercisable as of December 31, 2022	<u>2,750,625</u>	\$ 21.69	6.86	\$ 570
Vested and expected to vest as of December 31, 2022	<u>6,993,052</u>	\$ 21.57	7.78	\$ 1,031

Other information related to the option activity of the Company was as follows:

	Years Ended December 31,	
	2022	2021
Weighted-average fair value of options granted	\$ 13.44	\$ 29.54
Intrinsic value of options exercised (in thousands)	\$ 1,796	\$ 17,321

As of December 31, 2022, the unrecognized compensation cost related to outstanding options was \$58.4 million, which is expected to be recognized over a weighted-average period of 2.5 years.

The following table summarizes assumptions used in the Black-Scholes option pricing model to determine the fair value of stock options granted to employees:

	Years Ended December 31,	
	2022	2021
Expected option life (years)	5.50 - 6.11	5.50 - 6.11
Risk-free interest rate	1.47% - 4.22%	0.59% - 1.34%
Expected volatility	81.36% - 88.75%	80.45% - 86.20%
Expected dividend yield	0.00%	0.00%

***Performance-based restricted stock units***

In January and February 2022, the Company's Board of Directors authorized an issuance of 563,500 restricted stock units, or RSUs, to certain employees, including members of the Company's leadership team under the 2020 Plan. Vesting of the RSUs are contingent upon the determination of achievement of certain discovery and clinical milestones, or as specified market conditions are met. Upon vesting, each RSU converts automatically into one share of the Company's common stock.

**C4 Therapeutics, Inc.**
**Notes to Consolidated Financial Statements — Continued**

The following table summarizes the activity under the Company's equity plans with respect to RSUs for the year ended December 31, 2022:

	Shares	Weighted-Average Grant Date Fair Value
Outstanding as of December 31, 2021	—	\$ —
Granted	563,500	25.47
Vested <sup>(1)</sup>	(64,383)	25.01
Forfeited	(33,826)	31.58
Outstanding as of December 31, 2022	<u>465,291</u>	<u>\$ 25.09</u>

<sup>(1)</sup> Vested RSUs include 10,287 shares retained by the Company to cover statutory minimum withholding taxes.

As of December 31, 2022, the unrecognized compensation cost related to outstanding RSUs was \$10.1 million.

**2020 Employee Stock Purchase Plan**

In September 2020, the Company's Board of Directors adopted the C4 Therapeutics, Inc. 2020 Employee Stock Purchase Plan, or the 2020 ESPP. Eligible employees may authorize payroll deductions of up to 15% of their eligible compensation during an offering period. The Company may hold one or more offering periods each year during which employees will be able to purchase shares under the 2020 ESPP. The Company issued 31,402 shares during the year ended December 31, 2022.

As of December 31, 2022, the Company had 1,317,251 shares available for future issuance under the 2020 ESPP. The 2020 ESPP provides for an annual increase to be added on the first day of each fiscal year, beginning with January 1, 2021 and continuing thereafter through January 1, 2030, equal to the lesser of (i) 1% of the outstanding shares of common stock on the immediately preceding December 31st, (ii) 656,714 shares, or (ii) lesser number of shares determined by the administrator of the 2020 ESPP. On January 1, 2023, the annual increase for the 2020 ESPP resulted in an additional 489,662 shares authorized for issuance being added to the 2020 ESPP.

**Note 12. Income Taxes**

Income tax (benefit) expense consists of the following (in thousands):

	Years Ended December 31,	
	2022	2021
Current tax provision:		
Current federal provision	\$ —	\$ —
Current state provision	—	—
Total current provision	—	—
Deferred tax provision:		
Deferred federal provision	—	—
Deferred state provision	—	—
Total tax provision	<u>\$ —</u>	<u>\$ —</u>

## C4 Therapeutics, Inc.

## Notes to Consolidated Financial Statements — Continued

**Tax rate reconciliation**

A reconciliation of the expected income tax (benefit) expense computed at the statutory federal rate to income taxes as reflected in the consolidated financial statements was as follows:

	Years Ended December 31,	
	2022	2021
Income tax benefit computed at federal statutory tax rate	21.0 %	21.0 %
State tax—net of federal	8.0 %	6.0 %
Federal credits	1.4 %	3.1 %
State credits	0.1 %	1.7 %
Other permanent differences	(0.8)%	(0.3)%
Stock-based compensation	(3.0)%	(1.3)%
Valuation allowance	(26.7)%	(30.2)%
Total	— %	— %

**Significant components of deferred taxes**

Deferred income taxes reflect the net tax effects of (a) temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes and (b) operating losses and tax credit carryforwards. Significant components of the Company's deferred tax assets and deferred tax liabilities were as follows (in thousands):

	As of December 31,	
	2022	2021
Deferred tax assets:		
Net operating losses	\$ 54,300	\$ 46,339
Capitalized Research and Experimental Expenditures	27,568	—
Operating lease liability	21,443	9,290
R&D and investment tax credits	11,519	9,560
Deferred revenue	8,457	15,053
Stock-based compensation	6,296	3,675
Unrealized gain/loss	1,090	195
Capitalized start-up costs	699	875
Other	354	426
Total gross deferred tax assets	131,726	85,413
Deferred tax liabilities:		
Right-of-use asset	(19,868)	(9,242)
Fixed assets	(1,738)	(725)
Less: valuation allowance	(110,120)	(75,446)
Net deferred taxes	\$ —	\$ —

The Company has evaluated the positive and negative evidence bearing upon the realizability of the deferred tax assets. As of December 31, 2022 and 2021, based on the Company's historical operating losses, the Company has concluded that it is more-likely-than-not that the benefit of its deferred tax assets will not be realized. Accordingly, the Company has provided a full valuation allowance for the deferred tax assets as of December 31, 2022 and 2021. The valuation allowance for deferred tax assets as of December 31, 2022 and 2021 was \$110.1 million and \$75.4 million, respectively. The net valuation allowance increased \$34.7 million and \$25.6 million during the years ended December 31, 2022 and 2021, respectively. The change during the year ended December 31, 2022 was primarily due to the increase in net operating loss and tax credits carryforward, capitalization of research and experimental expenditures, and a decrease in deferred revenue recognized during the year.

## C4 Therapeutics, Inc.

## Notes to Consolidated Financial Statements — Continued

As of December 31, 2022 and 2021, the Company had \$171.6 million and \$152.2 million gross United States federal net operating loss, or NOL, carryforwards, respectively, which may be available to offset future income tax liabilities. The Tax Cuts and Jobs Act, or TCJA, which was enacted in December 2017, will generally allow federal losses generated after 2017 to be carried over indefinitely, but will generally limit the NOL deduction to the lesser of the NOL carryover or 80% of a corporation's taxable income (subject to Section 382 of the Internal Revenue Code of 1986, as amended, or IRC). In addition, there will be no carryback for losses generated after 2017. Losses generated prior to 2018 will generally be deductible to the extent of the lesser of a corporation's NOL carryover or 100% of a corporation's taxable income and be available for twenty years from the period the loss was generated. For U.S. federal income tax purposes, the Company has federal NOLs generated after 2017 of \$171.6 million, which do not expire. The Company does not have any available NOLs generated prior to 2019 as they were fully utilized in 2019. The Coronavirus Aid, Relief and Economic Security Act, or CARES Act, temporarily allows the Company to carryback net operating losses arising in 2018, 2019 and 2020 to the five prior tax years. In addition, net operating losses generated in these years could fully offset prior year taxable income without the 80% of the taxable income limitation under the TCJA.

As of December 31, 2022 and 2021, the Company has total gross United States state net operating loss carryforwards of \$273.6 million and \$216.8 million, respectively, which may be available to offset future income tax liabilities that expire at various dates through 2042.

At December 31, 2022 and 2021, the Company has United States federal research credit carryforwards of \$9.1 million and \$7.3 million, respectively, which are available to offset future federal income tax liabilities, which expire at various dates through 2042. At December 31, 2022 and 2021, the Company has United States state research credit carryforwards of \$2.9 million and \$2.9 million, respectively, which are available to reduce future tax liabilities which expire at various dates through 2037.

Net operating loss and tax credit carryforwards may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant stockholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the IRC, respectively, as well as similar state provisions. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of the Company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. In 2021, the Company completed a study of ownership changes from inception through December 31, 2020, to assess whether an ownership change has occurred or whether there have been multiple ownership changes since its formation. The result of this study indicated that the Company experienced ownership changes as defined by IRS Section 382 of the Code, however there are no net operating loss carryforwards that will be limited and expire unused as a result of such ownership changes. Given the continued loss position, the Company has not currently undertaken an analysis for IRC Section 382 purposes of any activities post December 31, 2020. A full valuation allowance has been provided against the Company's net operating loss and tax credit carryforwards and, if an adjustment is required, this adjustment would be offset by an adjustment to the valuation allowance.

The Company will recognize interest and/or penalties related to uncertain tax benefits in income tax expense as they arise. As of December 31, 2022 and 2021, the Company had no accrued interest or penalties related to uncertain tax benefits.

The Company files income tax returns in the United States, California, Florida, and Massachusetts. The federal and state income tax returns are generally subject to tax examinations for the tax years ended December 31, 2019 through present. To the extent that the Company has tax attribute carryforwards, the tax years in which the attributes were generated may still be adjusted upon examination by the Internal Revenue Services or State tax authorities to the extent utilized in a future period. The Company is not currently under examination by any tax authorities.

**Note 13. Net Loss per share**

As described in Note 2, *Summary of significant accounting policies*, for periods in which the Company reports a net loss, potentially dilutive securities have been excluded from the computation of diluted net loss per share as their effects would be anti-dilutive. Therefore, the weighted average number of common shares outstanding used to calculate both basic and diluted net loss per share is the same. The Company excluded the following potential common shares presented based on amounts outstanding at period end, from the computation of diluted net loss per share for the periods indicated because including them would have had an anti-dilutive effect:

	Years Ended December 31,	
	2022	2021
Options to purchase common stock	6,993,052	5,983,425



## C4 Therapeutics, Inc.

## Notes to Consolidated Financial Statements — Continued

Basic and diluted loss per share is computed by dividing net loss by the weighted-average common shares outstanding (in thousands, except share and per share data):

	Years Ended December 31,	
	2022	2021
<b>Numerator:</b>		
Net loss —basic and diluted	\$ (128,175)	\$ (83,892)
<b>Denominator:</b>		
Weighted-average common stock outstanding—basic and diluted	48,861,665	46,041,733
Net loss per share —basic and diluted	<u>\$ (2.62)</u>	<u>\$ (1.82)</u>

**Note 14. Defined contribution plan**

The Company has a 401(k) retirement plan, the 401(k) Plan, whereby all full-time employees may contribute up to 90% of their pre-tax compensation, up to the maximum allowable amount set by the Internal Revenue Service. The Company, at its discretion, matches 100% of contributions to the 401(k) Plan up to the IRS maximum per year for each full-time employee. During each of the years ended December 31, 2022 and 2021, the Company contributed approximately \$1.0 million and \$0.6 million, respectively, to the 401(k) Plan.

## C4 THERAPEUTICS, INC.

### 2020 STOCK OPTION AND INCENTIVE PLAN

#### SECTION 1. GENERAL PURPOSE OF THE PLAN; DEFINITIONS

The name of the plan is the C4 Therapeutics, Inc. 2020 Stock Option and Incentive Plan (the “**Plan**”). The purpose of the Plan is to encourage and enable the officers, employees, Non-Employee Directors and Consultants of C4 Therapeutics, Inc. (the “**Company**”) and its Affiliates upon whose judgment, initiative and efforts the Company largely depends for the successful conduct of its business to acquire a proprietary interest in the Company. It is anticipated that providing such persons with a direct stake in the Company’s welfare will assure a closer identification of their interests with those of the Company and its stockholders, thereby stimulating their efforts on the Company’s behalf and strengthening their desire to remain with the Company.

The following terms shall be defined as set forth below:

“**Act**” means the Securities Act of 1933, as amended, and the rules and regulations thereunder.

“**Administrator**” means either the Board or the compensation committee of the Board or a similar committee performing the functions of the compensation committee and which is comprised of not less than two Non-Employee Directors who are independent.

“**Affiliate**” means, at the time of determination, any “parent” or “subsidiary” of the Company as such terms are defined in Rule 405 of the Act. The Board will have the authority to determine the time or times at which “parent” or “subsidiary” status is determined within the foregoing definition.

“**Award**” or “**Awards**,” except where referring to a particular category of grant under the Plan, shall include Incentive Stock Options, Non-Qualified Stock Options, Stock Appreciation Rights, Restricted Stock Units, Restricted Stock Awards, Unrestricted Stock Awards, Cash-Based Awards and Dividend Equivalent Rights.

“**Award Certificate**” means a written or electronic document setting forth the terms and provisions applicable to an Award granted under the Plan. Each Award Certificate is subject to the terms and conditions of the Plan.

“**Board**” means the Board of Directors of the Company.

“**Cash-Based Award**” means an Award entitling the recipient to receive a cash-denominated payment.

“**Code**” means the Internal Revenue Code of 1986, as amended, and any successor Code, and related rules, regulations and interpretations.

“**Consultant**” means a consultant or adviser who provides *bona fide* services to the Company or an Affiliate as an independent contractor and who qualifies as a consultant or advisor under Instruction A.1.(a)(1) of Form S-8 under the Act.

“**Dividend Equivalent Right**” means an Award entitling the grantee to receive credits based on cash dividends that would have been paid on the shares of Stock specified in the

Dividend Equivalent Right (or other award to which it relates) if such shares had been issued to and held by the grantee.

“**Effective Date**” means the date on which the Plan becomes effective as set forth in Section 19.

“**Exchange Act**” means the Securities Exchange Act of 1934, as amended, and the rules and regulations thereunder.

“**Fair Market Value**” of the Stock on any given date means the fair market value of the Stock determined in good faith by the Administrator; *provided, however*, that if the Stock is listed on the Nasdaq Stock Market, The New York Stock Exchange or another national securities exchange or traded on any established market, the determination shall be made by reference to market quotations. If there are no market quotations for such date, the determination shall be made by reference to the last date preceding such date for which there are market quotations; *provided, further, however*, that if the date for which Fair Market Value is determined is the Registration Date, the Fair Market Value shall be the “Price to the Public” (or equivalent) set forth on the cover page for the final prospectus relating to the Company’s initial public offering.

“**Incentive Stock Option**” means any Stock Option designated and qualified as an “incentive stock option” as defined in Section 422 of the Code.

“**Non-Employee Director**” means a member of the Board who is not also an employee of the Company or any Subsidiary.

“**Non-Qualified Stock Option**” means any Stock Option that is not an Incentive Stock Option.

“**Option**” or “**Stock Option**” means any option to purchase shares of Stock granted pursuant to Section 5.

“**Registration Date**” means the date upon which the registration statement on Form S-1 that is filed by the Company with respect to its initial public offering is declared effective by the Securities and Exchange Commission.

“**Restricted Shares**” means the shares of Stock underlying a Restricted Stock Award that remain subject to a risk of forfeiture or the Company’s right of repurchase.

“**Restricted Stock Award**” means an Award of Restricted Shares subject to such restrictions and conditions as the Administrator may determine at the time of grant.

“**Restricted Stock Units**” means an Award of stock units subject to such restrictions and conditions as the Administrator may determine at the time of grant.

“**Sale Event**” shall mean (i) the sale of all or substantially all of the assets of the Company on a consolidated basis to an unrelated person or entity, (ii) a merger, reorganization or consolidation pursuant to which the holders of the Company’s outstanding voting power and outstanding stock immediately prior to such transaction do not own a majority of the outstanding voting power and outstanding stock or other equity interests of the resulting or successor entity (or its ultimate parent, if applicable) immediately upon completion of such transaction, (iii) the sale of all of the Stock of the Company to an unrelated person, entity or group thereof acting in concert, or (iv) any other transaction in which the owners of the Company’s outstanding voting power immediately prior to such transaction do not own at least a majority of the outstanding

voting power of the Company or any successor entity immediately upon completion of the transaction other than as a result of the acquisition of securities directly from the Company.

“**Sale Price**” means the value as determined by the Administrator of the consideration payable, or otherwise to be received by stockholders, per share of Stock pursuant to a Sale Event.

“**Section 409A**” means Section 409A of the Code and the regulations and other guidance promulgated thereunder.

“**Service Relationship**” means any relationship as an employee, director or Consultant of the Company or any Affiliate (e.g., a Service Relationship shall be deemed to continue without interruption in the event an individual’s status changes from full-time employee to part-time employee or Consultant or vice versa).

“**Stock**” means the Common Stock, par value \$0.0001 per share, of the Company, subject to adjustments pursuant to Section 3.

“**Stock Appreciation Right**” means an Award entitling the recipient to receive shares of Stock (or cash, to the extent explicitly provided for in the applicable Award Certificate) having a value equal to the excess of the Fair Market Value of the Stock on the date of exercise over the exercise price of the Stock Appreciation Right multiplied by the number of shares of Stock with respect to which the Stock Appreciation Right shall have been exercised.

“**Subsidiary**” means any corporation or other entity (other than the Company) in which the Company has at least a 50 percent interest, either directly or indirectly.

“**Ten Percent Owner**” means an employee who owns or is deemed to own (by reason of the attribution rules of Section 424(d) of the Code) more than 10 percent of the combined voting power of all classes of stock of the Company or any parent or subsidiary corporation.

“**Unrestricted Stock Award**” means an Award of shares of Stock free of any restrictions.

## SECTION 2. ADMINISTRATION OF PLAN; ADMINISTRATOR AUTHORITY TO SELECT GRANTEES AND DETERMINE AWARDS

(a) Administration of Plan. The Plan shall be administered by the Administrator.

(b) Powers of Administrator. The Administrator shall have the power and authority to grant Awards consistent with the terms of the Plan, including the power and authority:

(1) to select the individuals to whom Awards may from time to time be granted;

(2) to determine the time or times of grant, and the extent, if any, of Incentive Stock Options, Non-Qualified Stock Options, Stock Appreciation Rights, Restricted Stock Awards, Restricted Stock Units, Unrestricted Stock Awards, Cash-Based Awards and Dividend Equivalent Rights, or any combination of the foregoing, granted to any one or more grantees;

(3) to determine the number of shares of Stock to be covered by any Award;

(4) to determine and modify from time to time the terms and conditions, including restrictions, not inconsistent with the terms of the Plan, of any Award, which terms and

conditions may differ among individual Awards and grantees, and to approve the forms of Award Certificates;

(5) to accelerate at any time the exercisability or vesting of all or any portion of any Award;

(6) subject to the provisions of Section 5(c), to extend at any time the period in which Stock Options may be exercised; and

(7) at any time to adopt, alter and repeal such rules, guidelines and practices for administration of the Plan and for its own acts and proceedings as it shall deem advisable; to interpret the terms and provisions of the Plan and any Award (including related written instruments); to make all determinations it deems advisable for the administration of the Plan; to decide all disputes arising in connection with the Plan; and to otherwise supervise the administration of the Plan.

All decisions and interpretations of the Administrator shall be binding on all persons, including the Company and Plan grantees.

(c) Delegation of Authority to Grant Awards. Subject to applicable law, the Administrator, in its discretion, may delegate to a committee consisting of one or more officers of the Company, including the Chief Executive Officer, all or part of the Administrator's authority and duties with respect to the granting of Awards to individuals who are (i) not subject to the reporting and other provisions of Section 16 of the Exchange Act and (ii) not members of the delegated committee. Any such delegation by the Administrator shall include a limitation as to the amount of Stock underlying Awards that may be granted during the period of the delegation and shall contain guidelines as to the determination of the exercise price and the vesting criteria. The Administrator may revoke or amend the terms of a delegation at any time but such action shall not invalidate any prior actions of the Administrator's delegate or delegates that were consistent with the terms of the Plan.

(d) Award Certificate. Awards under the Plan shall be evidenced by Award Certificates that set forth the terms, conditions and limitations for each Award which may include, without limitation, the term of an Award and the provisions applicable in the event employment or service terminates.

(e) Indemnification. Neither the Board nor the Administrator, nor any member of either or any delegate thereof, shall be liable for any act, omission, interpretation, construction or determination made in good faith in connection with the Plan, and the members of the Board and the Administrator (and any delegate thereof) shall be entitled in all cases to indemnification and reimbursement by the Company in respect of any claim, loss, damage or expense (including, without limitation, reasonable attorneys' fees) arising or resulting therefrom to the fullest extent permitted by law and/or under the Company's certificate of incorporation or bylaws or any directors' and officers' liability insurance coverage which may be in effect from time to time and/or any indemnification agreement between such individual and the Company.

(f) Foreign Award Recipients. Notwithstanding any provision of the Plan to the contrary, in order to comply with the laws in other countries in which the Company and its Subsidiaries operate or have employees or other individuals eligible for Awards, the Administrator, in its sole discretion, shall have the power and authority to: (i) determine which Subsidiaries shall be covered by the Plan; (ii) determine which individuals outside the United States are eligible to participate in the Plan; (iii) modify the terms and conditions of any Award granted to individuals outside the United States to comply with applicable foreign laws; (iv) establish subplans and modify exercise procedures and other terms and procedures, to the extent

the Administrator determines such actions to be necessary or advisable (and such subplans and/or modifications shall be attached to this Plan as appendices); *provided, however*, that no such subplans and/or modifications shall increase the share limitations contained in Section 3(a) hereof; and (v) take any action, before or after an Award is made, that the Administrator determines to be necessary or advisable to obtain approval or comply with any local governmental regulatory exemptions or approvals. Notwithstanding the foregoing, the Administrator may not take any actions hereunder, and no Awards shall be granted, that would violate the Exchange Act or any other applicable United States securities law, the Code, or any other applicable United States governing statute or law.

### SECTION 3. STOCK ISSUABLE UNDER THE PLAN; MERGERS; SUBSTITUTION

(a) Stock Issuable. The maximum number of shares of Stock reserved and available for issuance under the Plan shall be 6,567,144 (the “**Initial Limit**”), subject to adjustment as provided in Section 3(c), plus on January 1, 2021 and each January 1 thereafter, the number of shares of Stock reserved and available for issuance under the Plan shall be cumulatively increased by the lesser of (i) five percent (5%) of the number of shares of Stock issued and outstanding on the immediately preceding December 31 or (ii) such lesser number of shares as determined by the Administrator (the “**Annual Increase**”). Subject to such overall limitation, the maximum aggregate number of shares of Stock that may be issued in the form of Incentive Stock Options under this Plan shall not exceed the Initial Limit cumulatively increased on January 1, 2021 and on each January 1 thereafter by the lesser of the Annual Increase for such year or 6,567,144 shares of Stock, subject in all cases to adjustment as provided in Section 3(c). For purposes of this limitation, the shares of Stock underlying any awards under the Plan and under the Company’s 2015 Stock Option and Grant Plan that are forfeited, canceled, held back upon exercise of an Option or settlement of an Award to cover the exercise price or tax withholding, reacquired by the Company prior to vesting, satisfied without the issuance of Stock or otherwise terminated (other than by exercise) shall be added back to the shares of Stock available for issuance under the Plan and, to the extent permitted under Section 422 of the Code and the regulations promulgated thereunder, the shares of Stock that may be issued as Incentive Stock Options. If the Company repurchases shares of Stock on the open market, such shares shall not be added to the shares of Stock available for issuance under the Plan. Subject to such overall limitations, shares of Stock may be issued up to such maximum number pursuant to any type or types of Award. The shares available for issuance under the Plan may be authorized but unissued shares of Stock or shares of Stock reacquired by the Company.

(b) Maximum Awards to Non-Employee Directors. Notwithstanding anything to the contrary in this Plan, the value of all Awards awarded under this Plan and all other cash compensation paid by the Company to any Non-Employee Director in any calendar year shall not exceed \$750,000; *provided, however*, that such amount shall be \$1,500,000 for the calendar year in which the applicable Non-Employee Director is initially elected or appointed to the Board. For the purpose of this limitation, the value of any Award shall be its grant date fair value, as determined in accordance with ASC 718 or successor provision but excluding the impact of estimated forfeitures related to service-based vesting provisions.

(c) Changes in Stock. Subject to Section 3(d) hereof, if, as a result of any reorganization, recapitalization, reclassification, stock dividend, stock split, reverse stock split or other similar change in the Company’s capital stock, the outstanding shares of Stock are increased or decreased or are exchanged for a different number or kind of shares or other securities of the Company, or additional shares or new or different shares or other securities of the Company or other non-cash assets are distributed with respect to such shares of Stock or other securities, or, if, as a result of any merger or consolidation, sale of all or substantially all of the assets of the Company, the outstanding shares of Stock are converted into or exchanged for securities of the Company or any successor entity (or a parent or subsidiary thereof), the

Administrator shall make an appropriate or proportionate adjustment in (i) the maximum number of shares reserved for issuance under the Plan, including the maximum number of shares that may be issued in the form of Incentive Stock Options; (ii) the number and kind of shares or other securities subject to any then outstanding Awards under the Plan; (iii) the repurchase price, if any, per share subject to each outstanding Restricted Stock Award; and (iv) the exercise price for each share subject to any then outstanding Stock Options and Stock Appreciation Rights under the Plan, without changing the aggregate exercise price (i.e., the exercise price multiplied by the number of shares subject to Stock Options and Stock Appreciation Rights) as to which such Stock Options and Stock Appreciation Rights remain exercisable. The Administrator shall also make equitable or proportionate adjustments in the number of shares subject to outstanding Awards and the exercise price and the terms of outstanding Awards to take into consideration cash dividends paid other than in the ordinary course or any other extraordinary corporate event. The adjustment by the Administrator shall be final, binding and conclusive. No fractional shares of Stock shall be issued under the Plan resulting from any such adjustment, but the Administrator in its discretion may make a cash payment in lieu of fractional shares.

(d) Mergers and Other Transactions. In the case of and subject to the consummation of a Sale Event, the parties thereto may cause the assumption or continuation of Awards theretofore granted by the successor entity, or the substitution of such Awards with new Awards of the successor entity or parent thereof, with appropriate adjustment as to the number and kind of shares and, if appropriate, the per share exercise prices, as such parties shall agree. To the extent the parties to such Sale Event do not provide for the assumption, continuation or substitution of Awards, upon the effective time of the Sale Event, the Plan and all outstanding Awards granted hereunder shall terminate. In such case, except as may be otherwise provided in the relevant Award Certificate, all Options and Stock Appreciation Rights with time-based vesting conditions or restrictions that are not vested and/or exercisable immediately prior to the effective time of the Sale Event shall become fully vested and exercisable as of the effective time of the Sale Event, all other Awards with time-based vesting, conditions or restrictions shall become fully vested and nonforfeitable as of the effective time of the Sale Event, and all Awards with conditions and restrictions relating to the attainment of performance goals may become vested and nonforfeitable in connection with a Sale Event in the Administrator's discretion or to the extent specified in the relevant Award Certificate. In the event of such termination, (i) the Company shall have the option (in its sole discretion) to make or provide for a payment, in cash or in kind, to the grantees holding Options and Stock Appreciation Rights, in exchange for the cancellation thereof, in an amount equal to the difference between (A) the Sale Price multiplied by the number of shares of Stock subject to outstanding Options and Stock Appreciation Rights (to the extent then exercisable at prices not in excess of the Sale Price) and (B) the aggregate exercise price of all such outstanding Options and Stock Appreciation Rights (*provided* that, in the case of an Option or Stock Appreciation Right with an exercise price equal to or less than the Sale Price, such Option or Stock Appreciation Right shall be cancelled for no consideration); or (ii) each grantee shall be permitted, within a specified period of time prior to the consummation of the Sale Event as determined by the Administrator, to exercise all outstanding Options and Stock Appreciation Rights (to the extent then exercisable) held by such grantee. The Company shall also have the option (in its sole discretion) to make or provide for a payment, in cash or in kind, to the grantees holding other Awards in an amount equal to the Sale Price multiplied by the number of vested shares of Stock under such Awards.

#### SECTION 4. ELIGIBILITY

Grantees under the Plan will be such employees, Non-Employee Directors and Consultants of the Company and its Affiliates as are selected from time to time by the Administrator in its sole discretion; *provided* that Awards may not be granted to employees, Directors or Consultants who are providing services only to any "parent" of the Company, as such term is defined in Rule 405 of the Act, unless (i) the stock underlying the Awards is treated

as “service recipient stock” under Section 409A or (ii) the Company has determined that such Awards are exempt from or otherwise comply with Section 409A.

## SECTION 5. STOCK OPTIONS

(a) Award of Stock Options. The Administrator may grant Stock Options under the Plan. Any Stock Option granted under the Plan shall be in such form as the Administrator may from time to time approve.

Stock Options granted under the Plan may be either Incentive Stock Options or Non-Qualified Stock Options. Incentive Stock Options may be granted only to employees of the Company or any Subsidiary that is a “subsidiary corporation” within the meaning of Section 424(f) of the Code. To the extent that any Option, or any portion thereof, does not qualify as an Incentive Stock Option, it shall be deemed a Non-Qualified Stock Option.

Stock Options granted pursuant to this Section 5 shall be subject to the following terms and conditions and shall contain such additional terms and conditions, not inconsistent with the terms of the Plan, as the Administrator shall deem desirable. If the Administrator so determines, Stock Options may be granted in lieu of cash compensation at the optionee’s election, subject to such terms and conditions as the Administrator may establish.

(b) Exercise Price. The exercise price per share for the Stock covered by a Stock Option granted pursuant to this Section 5 shall be determined by the Administrator at the time of grant but shall not be less than one hundred percent (100%) of the Fair Market Value on the date of grant. In the case of an Incentive Stock Option that is granted to a Ten Percent Owner, the exercise price of such Incentive Stock Option shall be not less than one hundred and ten percent (110%) of the Fair Market Value on the grant date. Notwithstanding the foregoing, Stock Options may be granted with an exercise price per share that is less than one hundred percent (100%) of the Fair Market Value on the date of grant (i) pursuant to a transaction described in, and in a manner consistent with, Section 424(a) of the Code, (ii) to individuals who are not subject to U.S. income tax on the date of grant, or (iii) the Stock Option is otherwise compliant with Section 409A.

(c) Option Term. The term of each Stock Option shall be fixed by the Administrator, but no Stock Option shall be exercisable more than ten years after the date the Stock Option is granted. In the case of an Incentive Stock Option that is granted to a Ten Percent Owner, the term of such Stock Option shall be no more than five years from the date of grant.

(d) Exercisability; Rights of a Stockholder. Stock Options shall become exercisable at such time or times, whether or not in installments, as shall be determined by the Administrator at or after the grant date. The Administrator may at any time accelerate the exercisability of all or any portion of any Stock Option. An optionee shall have the rights of a stockholder only as to shares acquired upon the exercise of a Stock Option and not as to unexercised Stock Options.

(e) Method of Exercise. Stock Options may be exercised in whole or in part, by giving written or electronic notice of exercise to the Company, specifying the number of shares to be purchased. Payment of the purchase price may be made by one or more of the following methods except to the extent otherwise provided in the Option Award Certificate:

(1) In cash, by certified or bank check or other instrument acceptable to the Administrator;

(2) Through the delivery (or attestation to the ownership following such procedures as the Company may prescribe) of shares of Stock that are not then subject to



restrictions under any Company plan. Such surrendered shares shall be valued at Fair Market Value on the exercise date;

(3) By the optionee delivering to the Company a properly executed exercise notice together with irrevocable instructions to a broker to promptly deliver to the Company cash or a check payable and acceptable to the Company for the purchase price; *provided* that in the event the optionee chooses to pay the purchase price as so provided, the optionee and the broker shall comply with such procedures and enter into such agreements of indemnity and other agreements as the Company shall prescribe as a condition of such payment procedure; or

(4) With respect to Stock Options that are not Incentive Stock Options, by a “net exercise” arrangement pursuant to which the Company will reduce the number of shares of Stock issuable upon exercise by the largest whole number of shares with a Fair Market Value that does not exceed the aggregate exercise price.

Payment instruments will be received subject to collection. The transfer to the optionee on the records of the Company or of the transfer agent of the shares of Stock to be purchased pursuant to the exercise of a Stock Option will be contingent upon receipt from the optionee (or a purchaser acting in his stead in accordance with the provisions of the Stock Option) by the Company of the full purchase price for such shares and the fulfillment of any other requirements contained in the Option Award Certificate or applicable provisions of laws (including the satisfaction of any withholding taxes that the Company is obligated to withhold with respect to the optionee). In the event an optionee chooses to pay the purchase price by previously-owned shares of Stock through the attestation method, the number of shares of Stock transferred to the optionee upon the exercise of the Stock Option shall be net of the number of attested shares. In the event that the Company establishes, for itself or using the services of a third party, an automated system for the exercise of Stock Options, such as a system using an internet website or interactive voice response, then the paperless exercise of Stock Options may be permitted through the use of such an automated system.

(f) Annual Limit on Incentive Stock Options. To the extent required for “incentive stock option” treatment under Section 422 of the Code, the aggregate Fair Market Value (determined as of the time of grant) of the shares of Stock with respect to which Incentive Stock Options granted under this Plan and any other plan of the Company or its parent and subsidiary corporations become exercisable for the first time by an optionee during any calendar year shall not exceed \$100,000. To the extent that any Stock Option exceeds this limit, it shall constitute a Non-Qualified Stock Option.

## SECTION 6.

### STOCK APPRECIATION RIGHTS

(a) Award of Stock Appreciation Rights. The Administrator may grant Stock Appreciation Rights under the Plan. A Stock Appreciation Right is an Award entitling the recipient to receive shares of Stock (or cash, to the extent explicitly provided for in the applicable Award Certificate) having a value equal to the excess of the Fair Market Value of a share of Stock on the date of exercise over the exercise price of the Stock Appreciation Right multiplied by the number of shares of Stock with respect to which the Stock Appreciation Right shall have been exercised.

(b) Exercise Price of Stock Appreciation Rights. The exercise price of a Stock Appreciation Right shall not be less than one hundred percent (100%) of the Fair Market Value of the Stock on the date of grant.

(c) Grant and Exercise of Stock Appreciation Rights. Stock Appreciation Rights may be granted by the Administrator independently of any Stock Option granted pursuant to Section 5 of the Plan.

(d) Terms and Conditions of Stock Appreciation Rights. Stock Appreciation Rights shall be subject to such terms and conditions as shall be determined on the date of grant by the Administrator. The term of a Stock Appreciation Right may not exceed ten years. The terms and conditions of each such Award shall be determined by the Administrator, and such terms and conditions may differ among individual Awards and grantees.

## SECTION 7. RESTRICTED STOCK AWARDS

(a) Nature of Restricted Stock Awards. The Administrator may grant Restricted Stock Awards under the Plan. A Restricted Stock Award is any Award of Restricted Shares subject to such restrictions and conditions as the Administrator may determine at the time of grant. Conditions may be based on continuing employment (or other Service Relationship) and/or achievement of pre-established performance goals and objectives.

(b) Rights as a Stockholder. Upon the grant of the Restricted Stock Award and payment of any applicable purchase price, a grantee shall have the rights of a stockholder with respect to the voting of the Restricted Shares and receipt of dividends; *provided* that if the lapse of restrictions with respect to the Restricted Stock Award is tied to the attainment of performance goals, any dividends paid by the Company during the performance period shall accrue and shall not be paid to the grantee until and to the extent the performance goals are met with respect to the Restricted Stock Award. Unless the Administrator shall otherwise determine, (i) uncertificated Restricted Shares shall be accompanied by a notation on the records of the Company or the transfer agent to the effect that they are subject to forfeiture until such Restricted Shares are vested as provided in Section 7(d) below, and (ii) certificated Restricted Shares shall remain in the possession of the Company until such Restricted Shares are vested as provided in Section 7(d) below, and the grantee shall be required, as a condition of the grant, to deliver to the Company such instruments of transfer as the Administrator may prescribe.

(c) Restrictions. Restricted Shares may not be sold, assigned, transferred, pledged or otherwise encumbered or disposed of except as specifically provided herein or in the Restricted Stock Award Certificate. Except as may otherwise be provided by the Administrator either in the Award Certificate or, subject to Section 16 below, in writing after the Award is issued, if a grantee's employment (or other Service Relationship) with the Company and its Subsidiaries terminates for any reason, any Restricted Shares that have not vested at the time of termination shall automatically and without any requirement of notice to such grantee from or other action by or on behalf of, the Company be deemed to have been reacquired by the Company at its original purchase price (if any) from such grantee or such grantee's legal representative simultaneously with such termination of employment (or other Service Relationship), and thereafter shall cease to represent any ownership of the Company by the grantee or rights of the grantee as a stockholder. Following such deemed reacquisition of Restricted Shares that are represented by physical certificates, a grantee shall surrender such certificates to the Company upon request without consideration.

(d) Vesting of Restricted Shares. The Administrator at the time of grant shall specify the date or dates and/or the attainment of pre-established performance goals, objectives and other conditions on which the non-transferability of the Restricted Shares and the Company's right of repurchase or forfeiture shall lapse. Subsequent to such date or dates and/or the attainment of such pre-established performance goals, objectives and other conditions, the shares on which all restrictions have lapsed shall no longer be Restricted Shares and shall be deemed "vested."

## SECTION 8.

### RESTRICTED STOCK UNITS

(a) Nature of Restricted Stock Units. The Administrator may grant Restricted Stock Units under the Plan. A Restricted Stock Unit is an Award of stock units that may be settled in shares of Stock (or cash, to the extent explicitly provided for in the Award Certificate) upon the satisfaction of such restrictions and conditions at the time of grant. Conditions may be based on continuing employment (or other Service Relationship) and/or achievement of pre-established performance goals and objectives. The terms and conditions of each such Award shall be determined by the Administrator, and such terms and conditions may differ among individual Awards and grantees. Except in the case of Restricted Stock Units with a deferred settlement date that complies with Section 409A, at the end of the vesting period, the Restricted Stock Units, to the extent vested, shall be settled in the form of shares of Stock. Restricted Stock Units with deferred settlement dates are subject to Section 409A and shall contain such additional terms and conditions as the Administrator shall determine in its sole discretion in order to comply with the requirements of Section 409A.

(b) Election to Receive Restricted Stock Units in Lieu of Compensation. The Administrator may, in its sole discretion, permit a grantee to elect to receive a portion of future cash compensation otherwise due to such grantee in the form of an award of Restricted Stock Units. Any such election shall be made in writing and shall be delivered to the Company no later than the date specified by the Administrator and in accordance with Section 409A and such other rules and procedures established by the Administrator. Any such future cash compensation that the grantee elects to defer shall be converted to a fixed number of Restricted Stock Units based on the Fair Market Value of Stock on the date the compensation would otherwise have been paid to the grantee if such payment had not been deferred as provided herein. The Administrator shall have the sole right to determine whether and under what circumstances to permit such elections and to impose such limitations and other terms and conditions thereon as the Administrator deems appropriate. Any Restricted Stock Units that are elected to be received in lieu of cash compensation shall be fully vested, unless otherwise provided in the Award Certificate.

(c) Rights as a Stockholder. A grantee shall have the rights as a stockholder only as to shares of Stock acquired by the grantee upon settlement of Restricted Stock Units; *provided, however*, that the grantee may be credited with Dividend Equivalent Rights with respect to the stock units underlying his Restricted Stock Units, subject to the provisions of Section 11 and such terms and conditions as the Administrator may determine.

(d) Termination. Except as may otherwise be provided by the Administrator either in the Award Certificate or, subject to Section 16 below, in writing after the Award is issued, a grantee's right in all Restricted Stock Units that have not vested shall automatically terminate upon the grantee's termination of employment (or cessation of Service Relationship) with the Company and its Subsidiaries for any reason.

## SECTION 9.

### UNRESTRICTED STOCK AWARDS

Grant or Sale of Unrestricted Stock. The Administrator may grant (or sell at par value or such higher purchase price determined by the Administrator) an Unrestricted Stock Award under the Plan. An Unrestricted Stock Award is an Award pursuant to which the grantee may receive shares of Stock free of any restrictions under the Plan. Unrestricted Stock Awards may be granted in respect of past services or other valid consideration, or in lieu of cash compensation due to such grantee.

## SECTION 10.

### CASH-BASED AWARDS

Grant of Cash-Based Awards. The Administrator may grant Cash-Based Awards under the Plan. A Cash-Based Award is an Award that entitles the grantee to a payment in cash upon the attainment of specified performance goals. The Administrator shall determine the maximum duration of the Cash-Based Award, the amount of cash to which the Cash-Based Award pertains, the conditions upon which the Cash-Based Award shall become vested or payable, and such other provisions as the Administrator shall determine. Each Cash-Based Award shall specify a cash-denominated payment amount, formula or payment ranges as determined by the Administrator. Payment, if any, with respect to a Cash-Based Award shall be made in accordance with the terms of the Award and may be made in cash.

## SECTION 11.

### DIVIDEND EQUIVALENT RIGHTS

(a) Dividend Equivalent Rights. The Administrator may grant Dividend Equivalent Rights under the Plan. A Dividend Equivalent Right is an Award entitling the grantee to receive credits based on cash dividends that would have been paid on the shares of Stock specified in the Dividend Equivalent Right (or other Award to which it relates) if such shares had been issued to the grantee. A Dividend Equivalent Right may be granted hereunder to any grantee as a component of an award of Restricted Stock Units or as a freestanding award. The terms and conditions of Dividend Equivalent Rights shall be specified in the Award Certificate. Dividend equivalents credited to the holder of a Dividend Equivalent Right may be paid currently or may be deemed to be reinvested in additional shares of Stock, which may thereafter accrue additional equivalents. Any such reinvestment shall be at Fair Market Value on the date of reinvestment or such other price as may then apply under a dividend reinvestment plan sponsored by the Company, if any. Dividend Equivalent Rights may be settled in cash or shares of Stock or a combination thereof, in a single installment or installments. A Dividend Equivalent Right granted as a component of an Award of Restricted Stock Units shall provide that such Dividend Equivalent Right shall be settled only upon settlement or payment of, or lapse of restrictions on, such other Award, and that such Dividend Equivalent Right shall expire or be forfeited or annulled under the same conditions as such other Award.

(b) Termination. Except as may otherwise be provided by the Administrator either in the Award Certificate or, subject to Section 16 below, in writing after the Award is issued, a grantee's rights in all Dividend Equivalent Rights shall automatically terminate upon the grantee's termination of employment (or cessation of Service Relationship) with the Company and its Subsidiaries for any reason.

## SECTION 12.

### TRANSFERABILITY OF AWARDS

(a) Transferability. Except as provided in Section 12(b) below, during a grantee's lifetime, his or her Awards shall be exercisable only by the grantee, or by the grantee's legal representative or guardian in the event of the grantee's incapacity. No Awards shall be sold, assigned, transferred or otherwise encumbered or disposed of by a grantee other than by will or by the laws of descent and distribution or pursuant to a domestic relations order. No Awards shall be subject, in whole or in part, to attachment, execution, or levy of any kind, and any purported transfer in violation hereof shall be null and void.

(b) Administrator Action. Notwithstanding Section 12(a), the Administrator, in its discretion, may provide either in the Award Certificate regarding a given Award or by subsequent written approval that the grantee (who is an employee or director) may transfer his or her Non-Qualified Stock Options to his or her immediate family members, to trusts for the benefit of such family members, or to partnerships in which such family members are the only partners, *provided* that the transferee agrees in writing with the Company to be bound by all of

the terms and conditions of this Plan and the applicable Award. In no event may an Award be transferred by a grantee for value.

(c) Family Member. For purposes of Section 12(b), “**family member**” shall mean a grantee’s child, stepchild, grandchild, parent, stepparent, grandparent, spouse, former spouse, sibling, niece, nephew, mother-in-law, father-in-law, son-in-law, daughter-in-law, brother-in-law, or sister-in-law, including adoptive relationships, any person sharing the grantee’s household (other than a tenant of the grantee), a trust in which these persons (or the grantee) have more than 50 percent of the beneficial interest, a foundation in which these persons (or the grantee) control the management of assets, and any other entity in which these persons (or the grantee) own more than 50 percent of the voting interests.

(d) Designation of Beneficiary. To the extent permitted by the Company, each grantee to whom an Award has been made under the Plan may designate a beneficiary or beneficiaries to exercise any Award or receive any payment under any Award payable on or after the grantee’s death. Any such designation shall be on a form provided for that purpose by the Administrator and shall not be effective until received by the Administrator. If no beneficiary has been designated by a deceased grantee, or if the designated beneficiaries have predeceased the grantee, the beneficiary shall be the grantee’s estate.

#### SECTION 13. TAX WITHHOLDING

(a) Payment by Grantee. Each grantee shall, no later than the date as of which the value of an Award or of any Stock or other amounts received thereunder first becomes includable in the gross income of the grantee for income tax purposes, pay to the Company, or make arrangements satisfactory to the Administrator regarding payment of, any Federal, state, or local taxes of any kind required by law to be withheld by the Company with respect to such income. The Company and its Subsidiaries shall, to the extent permitted by law, have the right to deduct any such taxes from any payment of any kind otherwise due to the grantee. The Company’s obligation to deliver evidence of book entry (or stock certificates) to any grantee is subject to and conditioned on tax withholding obligations being satisfied by the grantee.

(b) Payment in Stock. The Administrator may require the Company’s tax withholding obligation to be satisfied, in whole or in part, by the Company withholding from shares of Stock to be issued pursuant to any Award a number of shares with an aggregate Fair Market Value (as of the date the withholding is effected) that would satisfy the withholding amount due; *provided, however*, that the amount withheld does not exceed the maximum statutory tax rate or such lesser amount as is necessary to avoid liability accounting treatment. For purposes of share withholding, the Fair Market Value of withheld shares shall be determined in the same manner as the value of Stock includible in income of the grantee. The Administrator may also require the Company’s tax withholding obligation to be satisfied, in whole or in part, by an arrangement whereby a certain number of shares of Stock issued pursuant to any Award are immediately sold and proceeds from such sale are remitted to the Company in an amount that would satisfy the withholding amount due.

#### SECTION 14. SECTION 409A AWARDS

Awards are intended to be exempt from Section 409A to the greatest extent possible and to otherwise comply with Section 409A. The Plan and all Awards shall be interpreted in accordance with such intent. To the extent that any Award is determined to constitute “nonqualified deferred compensation” within the meaning of Section 409A (a “**409A Award**”), the Award shall be subject to such additional rules and requirements as specified by the Administrator from time to time in order to comply with Section 409A. In this regard, if any amount under a 409A Award is payable upon a “separation from service” (within the meaning of

Section 409A) to a grantee who is then considered a “specified employee” (within the meaning of Section 409A), then no such payment shall be made prior to the date that is the earlier of (i) six months and one day after the grantee’s separation from service, or (ii) the grantee’s death, but only to the extent such delay is necessary to prevent such payment from being subject to interest, penalties and/or additional tax imposed pursuant to Section 409A. Further, the settlement of any 409A Award may not be accelerated except to the extent permitted by Section 409A.

#### SECTION 15. TERMINATION OF SERVICE RELATIONSHIP, TRANSFER, LEAVE OF ABSENCE, ETC.

(a) Termination of Service Relationship. If the grantee’s Service Relationship is with an Affiliate and such Affiliate ceases to be an Affiliate, the grantee shall be deemed to have terminated his or her Service Relationship for purposes of the Plan.

(b) For purposes of the Plan, the following events shall not be deemed a termination of a Service Relationship:

(1) a transfer to the employment of the Company from an Affiliate or from the Company to an Affiliate, or from one Affiliate to another; or

(2) an approved leave of absence for military service or sickness, or for any other purpose approved by the Company, if the employee’s right to re-employment is guaranteed either by a statute or by contract or under the policy pursuant to which the leave of absence was granted or if the Administrator otherwise so provides in writing.

#### SECTION 16. AMENDMENTS AND TERMINATION

The Board may, at any time, amend or discontinue the Plan and the Administrator may, at any time, amend or cancel any outstanding Award for the purpose of satisfying changes in law or for any other lawful purpose, but no such action shall materially and adversely affect rights under any outstanding Award without the holder’s consent. The Administrator is specifically authorized to exercise its discretion to reduce the exercise price of outstanding Stock Options or Stock Appreciation Rights or effect the repricing of such Awards through cancellation and re-grants. To the extent required under the rules of any securities exchange or market system on which the Stock is listed, to the extent determined by the Administrator to be required by the Code to ensure that Incentive Stock Options granted under the Plan are qualified under Section 422 of the Code, Plan amendments shall be subject to approval by Company stockholders. Nothing in this Section 16 shall limit the Administrator’s authority to take any action permitted pursuant to Section 3(c) or 3(d).

#### SECTION 17. STATUS OF PLAN

With respect to the portion of any Award that has not been exercised and any payments in cash, Stock or other consideration not received by a grantee, a grantee shall have no rights greater than those of a general creditor of the Company unless the Administrator shall otherwise expressly determine in connection with any Award or Awards. In its sole discretion, the Administrator may authorize the creation of trusts or other arrangements to meet the Company’s obligations to deliver Stock or make payments with respect to Awards hereunder, *provided* that the existence of such trusts or other arrangements is consistent with the foregoing sentence.

- (a) No Distribution. The Administrator may require each person acquiring Stock pursuant to an Award to represent to and agree with the Company in writing that such person is acquiring the shares without a view to distribution thereof.
- (b) Issuance of Stock. To the extent certificated, stock certificates to grantees under this Plan shall be deemed delivered for all purposes when the Company or a stock transfer agent of the Company shall have mailed such certificates in the United States mail, addressed to the grantee, at the grantee's last known address on file with the Company. Uncertificated Stock shall be deemed delivered for all purposes when the Company or a Stock transfer agent of the Company shall have given to the grantee by electronic mail (with proof of receipt) or by United States mail, addressed to the grantee, at the grantee's last known address on file with the Company, notice of issuance and recorded the issuance in its records (which may include electronic "book entry" records). Notwithstanding anything herein to the contrary, the Company shall not be required to issue or deliver any evidence of book entry or certificates evidencing shares of Stock pursuant to the exercise or settlement of any Award, unless and until the Administrator has determined, with advice of counsel (to the extent the Administrator deems such advice necessary or advisable), that the issuance and delivery is in compliance with all applicable laws, regulations of governmental authorities and, if applicable, the requirements of any exchange on which the shares of Stock are listed, quoted or traded. Any Stock issued pursuant to the Plan shall be subject to any stop-transfer orders and other restrictions as the Administrator deems necessary or advisable to comply with federal, state or foreign jurisdiction, securities or other laws, rules and quotation system on which the Stock is listed, quoted or traded. The Administrator may place legends on any Stock certificate or notations on any book entry to reference restrictions applicable to the Stock. In addition to the terms and conditions provided herein, the Administrator may require that an individual make such reasonable covenants, agreements, and representations as the Administrator, in its discretion, deems necessary or advisable in order to comply with any such laws, regulations, or requirements. The Administrator shall have the right to require any individual to comply with any timing or other restrictions with respect to the settlement or exercise of any Award, including a window-period limitation, as may be imposed in the discretion of the Administrator.
- (c) Stockholder Rights. Until Stock is deemed delivered in accordance with Section 18(b), no right to vote or receive dividends or any other rights of a stockholder will exist with respect to shares of Stock to be issued in connection with an Award, notwithstanding the exercise of a Stock Option or any other action by the grantee with respect to an Award.
- (d) Other Compensation Arrangements; No Employment Rights. Nothing contained in this Plan shall prevent the Board from adopting other or additional compensation arrangements, including trusts, and such arrangements may be either generally applicable or applicable only in specific cases. The adoption of this Plan and the grant of Awards do not confer upon any employee any right to continued employment with the Company or any Subsidiary.
- (e) Trading Policy Restrictions. Option exercises and other Awards under the Plan shall be subject to the Company's insider trading policies and procedures, as in effect from time to time.
- (f) Clawback Policy. Awards under the Plan shall be subject to the Company's clawback policy, as in effect from time to time.

SECTION 19.

EFFECTIVE DATE OF PLAN

This Plan shall become effective upon the date immediately preceding the Registration Date subject to prior stockholder approval in accordance with applicable state law, the Company's bylaws and certificate of incorporation, and applicable stock exchange rules. No grants of Stock Options and other Awards may be made hereunder after the tenth anniversary of the Effective Date and no grants of Incentive Stock Options may be made hereunder after the tenth anniversary of the date the Plan is approved by the Board.

SECTION 20.

GOVERNING LAW

This Plan and all Awards and actions taken thereunder shall be governed by, and construed in accordance with, the General Corporation Law of the State of Delaware as to matters within the scope thereof, and as to all other matters shall be governed by, and construed in accordance with, the internal laws of the Commonwealth of Massachusetts, applied without regard to conflict of law principles.

DATE APPROVED BY BOARD OF DIRECTORS: September 8, 2020

DATE APPROVED BY STOCKHOLDERS: September 23, 2020

\* The share numbers in this Plan reflect the reverse stock split effected September 25, 2020.



**INCENTIVE STOCK OPTION AGREEMENT  
UNDER THE C4 THERAPEUTICS, INC.  
2020 STOCK OPTION AND INCENTIVE PLAN**

Name of Optionee: \_\_\_\_

No. of Option Shares: \_\_\_\_

Option Exercise Price per Share: \$\_\_\_\_  
[FMV on Grant Date (110% of FMV if a 10% owner)]

Grant Date: \_\_\_\_

Expiration Date: \_\_\_\_  
[up to 10 years (5 if a 10% owner)]

Pursuant to the C4 Therapeutics, Inc. 2020 Stock Option and Incentive Plan as amended through the date hereof (the “**Plan**”), C4 Therapeutics, Inc. (the “**Company**”) hereby grants to the Optionee named above an option (the “**Stock Option**”) to purchase on or prior to the Expiration Date specified above all or part of the number of shares of Common Stock, par value \$0.0001 per share (the “**Stock**”), of the Company specified above at the Option Exercise Price per Share specified above subject to the terms and conditions set forth herein and in the Plan.

1. Exercisability Schedule. No portion of this Stock Option may be exercised until such portion shall have become exercisable. Except as set forth below, and subject to the discretion of the Administrator (as defined in Section 2 of the Plan) to accelerate the exercisability schedule hereunder, this Stock Option shall be exercisable with respect to the following number of Option Shares on the dates indicated so long as the Optionee maintains a Service Relationship with the Company or a Subsidiary on each such date:

<u>Incremental Number of Option Shares Exercisable*</u>	<u>Exercisability Date</u>
_____ ( ____ %)	_____
_____ ( ____ %)	_____
_____ ( ____ %)	_____
_____ ( ____ %)	_____
_____ ( ____ %)	_____

\* Max. of \$100,000 per yr.

However, notwithstanding anything to the contrary, one hundred percent (100%) of the Option Shares shall immediately become exercisable upon the termination of the Optionee’s Service Relationship due to the Optionee’s death or disability (as determined by the Administrator).

Once exercisable, this Stock Option shall continue to be exercisable at any time or times prior to the close of business on the Expiration Date, subject to the provisions hereof and of the Plan.

2. Manner of Exercise.

(a) The Optionee may exercise this Stock Option only in the following manner: from time to time on or prior to the Expiration Date of this Stock Option, the Optionee may give written notice to the Administrator of his or her election to purchase some or all of the Option Shares purchasable at the time of such notice. This notice shall specify the number of Option Shares to be purchased.

Payment of the purchase price for the Option Shares may be made by one or more of the following methods: (i) in cash, by certified or bank check or other instrument acceptable to the Administrator; (ii) through the delivery (or attestation to the ownership) of shares of Stock that have been purchased by the Optionee on the open market or that are beneficially owned by the Optionee and are not then subject to any restrictions under any Company plan and that otherwise satisfy any holding periods as may be required by the Administrator; or (iii) by the Optionee delivering to the Company a properly executed exercise notice together with irrevocable instructions to a broker to promptly deliver to the Company cash or a check payable and acceptable to the Company to pay the option purchase price, *provided* that in the event the Optionee chooses to pay the option purchase price as so provided, the Optionee and the broker shall comply with such procedures and enter into such agreements of indemnity and other agreements as the Administrator shall prescribe as a condition of such payment procedure; or (iv) a combination of (i), (ii) and (iii) above. Payment instruments will be received subject to collection.

The transfer to the Optionee on the records of the Company or of the transfer agent of the Option Shares will be contingent upon (i) the Company's receipt from the Optionee of the full purchase price for the Option Shares, as set forth above, (ii) the fulfillment of any other requirements contained herein or in the Plan or in any other agreement or provision of laws, and (iii) the receipt by the Company of any agreement, statement or other evidence that the Company may require to satisfy itself that the issuance of Stock to be purchased pursuant to the exercise of Stock Options under the Plan and any subsequent resale of the shares of Stock will be in compliance with applicable laws and regulations. In the event the Optionee chooses to pay the purchase price by previously-owned shares of Stock through the attestation method, the number of shares of Stock transferred to the Optionee upon the exercise of the Stock Option shall be net of the Shares attested to.

(b) The shares of Stock purchased upon exercise of this Stock Option shall be transferred to the Optionee on the records of the Company or of the transfer agent upon compliance to the satisfaction of the Administrator with all requirements under applicable laws or regulations in connection with such transfer and with the requirements hereof and of the Plan. The determination of the Administrator as to such compliance shall be final and binding on the Optionee. The Optionee shall not be deemed to be the holder of, or to have any of the rights of a holder with respect to, any shares of Stock subject to this Stock Option unless and until this Stock Option shall have been exercised pursuant to the terms hereof, the Company or the transfer agent shall have transferred the shares to the Optionee, and the Optionee's name shall have been entered as the stockholder of record on the books of the Company. Thereupon, the Optionee shall have full voting, dividend and other ownership rights with respect to such shares of Stock.

(c) The minimum number of shares with respect to which this Stock Option may be exercised at any one time shall be 100 shares, unless the number of shares with respect to which this Stock Option is being exercised is the total number of shares subject to exercise under this Stock Option at the time.

(d) Notwithstanding any other provision hereof or of the Plan, no portion of this Stock Option shall be exercisable after the Expiration Date hereof.

3. Termination of Service Relationship. If the Optionee's employment by or other Service Relationship with the Company or a Subsidiary is terminated, the period within which to exercise the Stock Option may be subject to earlier termination as set forth below.

(a) Termination Due to Death. If the Optionee's employment or other Service Relationship with the Company or a Subsidiary terminates by reason of the Optionee's death, any portion of this Stock Option outstanding on the date of death may thereafter be exercised by the Optionee's legal representative or legatee for a period of 12 months from the date of death or until the Expiration Date, if earlier.

(b) Termination Due to Disability. If the Optionee's employment or other Service Relationship with the Company or a Subsidiary terminates by reason of the Optionee's disability (as determined by the Administrator), any portion of this Stock Option outstanding on the date on which the Optionee is determined to have a disability may thereafter be exercised by the Optionee for a period of 12 months from such date of disability or until the Expiration Date, if earlier.

(c) Termination for Cause. If the Optionee's employment or other Service Relationship with the Company or a Subsidiary terminates for Cause, any portion of this Stock Option outstanding on such date shall terminate immediately and be of no further force and effect. For purposes hereof, "Cause" shall mean, unless otherwise provided in an employment agreement between the Company and the Optionee, a determination by the Administrator that the Optionee shall be dismissed as a result of (i) any material breach by the Optionee of any agreement between the Optionee and the Company; (ii) the conviction of, indictment for or plea of nolo contendere by the Optionee to a felony or a crime involving moral turpitude; or (iii) any material misconduct or willful and deliberate non-performance (other than by reason of disability) by the Optionee of the Optionee's duties to the Company.

(d) Other Termination. If the Optionee's employment or other Service Relationship with the Company or a Subsidiary terminates for any reason other than the Optionee's death, disability, or Cause, and unless otherwise determined by the Administrator, any portion of this Stock Option outstanding on the date on which the Optionee's employment or other Service Relationship with the Company or a Subsidiary terminated may be exercised, to the extent exercisable on such date, for a period of three months from such date of termination or until the Expiration Date, if earlier. Any portion of this Stock Option that is not exercisable on the date of termination shall terminate immediately and be of no further force or effect.

The Administrator's determination of the reason for termination of the Optionee's employment or other Service Relationship with the Company or a Subsidiary shall be conclusive and binding on the Optionee and his or her representatives or legatees.

4. Incorporation of Plan. Notwithstanding anything herein to the contrary, this Stock Option shall be subject to and governed by all the terms and conditions of the Plan, including the powers of the Administrator set forth in Section 2(b) of the Plan. Capitalized terms in this Agreement shall have the meaning specified in the Plan, unless a different meaning is specified herein.

5. Transferability. This Agreement is personal to the Optionee, is non-assignable and is not transferable in any manner, by operation of law or otherwise, other than by will or the laws of descent and distribution. This Stock Option is exercisable, during the Optionee's lifetime, only by the Optionee, and thereafter, only by the Optionee's legal representative or legatee.

6. Status of the Stock Option. This Stock Option is intended to qualify as an “incentive stock option” under Section 422 of the Internal Revenue Code of 1986, as amended (the “Code”), but the Company does not represent or warrant that this Stock Option qualifies as such. The Optionee should consult with his or her own tax advisors regarding the tax effects of this Stock Option and the requirements necessary to obtain favorable income tax treatment under Section 422 of the Code, including, but not limited to, holding period requirements. To the extent any portion of this Stock Option does not so qualify as an “incentive stock option,” such portion shall be deemed to be a non-qualified stock option. If the Optionee intends to dispose or does dispose (whether by sale, gift, transfer or otherwise) of any Option Shares within the one-year period beginning on the date after the transfer of such shares to him or her, or within the two-year period beginning on the day after the grant of this Stock Option, he or she will so notify the Company within 30 days after such disposition.

7. Tax Withholding. The Optionee shall, not later than the date as of which the exercise of this Stock Option becomes a taxable event for Federal income tax purposes, pay to the Company or make arrangements satisfactory to the Administrator for payment of any Federal, state, and local taxes required by law to be withheld on account of such taxable event. The Company shall have the authority to cause the required tax withholding obligation to be satisfied, in whole or in part, by withholding from shares of Stock to be issued to the Optionee a number of shares of Stock with an aggregate Fair Market Value that would satisfy the withholding amount due.

8. No Obligation to Continue Service Relationship. Neither the Company nor any Subsidiary is obligated by or as a result of the Plan or this Agreement to continue the Optionee in employment or other Service Relationship with the Company or a Subsidiary and neither the Plan nor this Agreement shall interfere in any way with the right of the Company or any Subsidiary to terminate the Optionee’s employment or other Service Relationship with the Company or a Subsidiary at any time.

9. Integration. This Agreement constitutes the entire agreement between the parties with respect to this Stock Option and supersedes all prior agreements and discussions between the parties concerning such subject matter.

10. Data Privacy Consent. In order to administer the Plan and this Agreement and to implement or structure future equity grants, the Company, its subsidiaries and affiliates and certain agents thereof (together, the “**Relevant Companies**”) may process any and all personal or professional data, including but not limited to Social Security or other identification number, home address and telephone number, date of birth and other information that is necessary or desirable for the administration of the Plan and/or this Agreement (the “**Relevant Information**”). By entering into this Agreement, the Optionee (i) authorizes the Company to collect, process, register and transfer to the Relevant Companies all Relevant Information; (ii) waives any privacy rights the Optionee may have with respect to the Relevant Information; (iii) authorizes the Relevant Companies to store and transmit such information in electronic form; and (iv) authorizes the transfer of the Relevant Information to any jurisdiction in which the Relevant Companies consider appropriate. The Optionee shall have access to, and the right to change, the Relevant Information. Relevant Information will only be used in accordance with applicable law.

11. Notices. Notices hereunder shall be mailed or delivered to the Company at its principal place of business and shall be mailed or delivered to the Optionee at the address on file

with the Company or, in either case, at such other address as one party may subsequently furnish to the other party in writing.

**C4 THERAPEUTICS, INC.**

By: \_\_\_  
Title:

The foregoing Agreement is hereby accepted and the terms and conditions thereof hereby agreed to by the undersigned. Electronic acceptance of this Agreement pursuant to the Company's instructions to the Optionee (including through an online acceptance process) is acceptable.

Dated: \_\_\_ \_\_\_

Optionee's Signature

Optionee's name and address:

\_\_\_  
\_\_\_  
\_\_\_

**NON-QUALIFIED STOCK OPTION AGREEMENT  
FOR NON-EMPLOYEE CONSULTANTS  
UNDER THE C4 THERAPEUTICS, INC.  
2020 STOCK OPTION AND INCENTIVE PLAN**

Name of Optionee: \_\_\_\_

No. of Option Shares: \_\_\_\_

Option Exercise Price per Share: \$\_\_\_\_

[FMV on Grant Date]

Grant Date: \_\_\_\_

Expiration Date: \_\_\_\_

[No more than 10 years]

Pursuant to the C4 Therapeutics, Inc. 2020 Stock Option and Incentive Plan as amended through the date hereof (the “**Plan**”), C4 Therapeutics, Inc. (the “**Company**”) hereby grants to the Optionee named above, who is a Consultant of the Company, an option (the “**Stock Option**”) to purchase on or prior to the Expiration Date specified above all or part of the number of shares of Common Stock, par value \$0.0001 per share (the “**Stock**”), of the Company specified above at the Option Exercise Price per Share specified above subject to the terms and conditions set forth herein and in the Plan. This Stock Option is not intended to be an “incentive stock option” under Section 422 of the Internal Revenue Code of 1986, as amended.

1. Exercisability Schedule. No portion of this Stock Option may be exercised until such portion shall have become exercisable. Except as set forth below, and subject to the discretion of the Administrator (as defined in Section 2 of the Plan) to accelerate the exercisability schedule hereunder, this Stock Option shall be exercisable with respect to the following number of Option Shares on the dates indicated so long as the Optionee maintains a Service Relationship with the Company or a Subsidiary on each such date:

<u>Incremental Number of Option Shares Exercisable</u>	<u>Exercisability Date</u>
_____ ( ____ %)	_____
_____ ( ____ %)	_____
_____ ( ____ %)	_____
_____ ( ____ %)	_____
_____ ( ____ %)	_____

However, notwithstanding anything to the contrary, one hundred percent (100%) of the Option Shares shall immediately become exercisable upon the termination of the Optionee’s Service Relationship due to the Optionee’s death or disability (as determined by the Administrator).

Once exercisable, this Stock Option shall continue to be exercisable at any time or times prior to the close of business on the Expiration Date, subject to the provisions hereof and of the Plan.

2. Manner of Exercise.

(a) The Optionee may exercise this Stock Option only in the following manner: from time to time on or prior to the Expiration Date of this Stock Option, the Optionee may give written notice to the Administrator of his or her election to purchase some or all of the Option Shares purchasable at the time of such notice. This notice shall specify the number of Option Shares to be purchased.

Payment of the purchase price for the Option Shares may be made by one or more of the following methods: (i) in cash, by certified or bank check or other instrument acceptable to the Administrator; (ii) through the delivery (or attestation to the ownership) of shares of Stock that have been purchased by the Optionee on the open market or that are beneficially owned by the Optionee and are not then subject to any restrictions under any Company plan and that otherwise satisfy any holding periods as may be required by the Administrator; (iii) by the Optionee delivering to the Company a properly executed exercise notice together with irrevocable instructions to a broker to promptly deliver to the Company cash or a check payable and acceptable to the Company to pay the option purchase price, *provided* that in the event the Optionee chooses to pay the option purchase price as so provided, the Optionee and the broker shall comply with such procedures and enter into such agreements of indemnity and other agreements as the Administrator shall prescribe as a condition of such payment procedure; (iv) by a “net exercise” arrangement pursuant to which the Company will reduce the number of shares of Stock issuable upon exercise by the largest whole number of shares with a Fair Market Value that does not exceed the aggregate exercise price; or (v) a combination of (i), (ii), (iii) and (iv) above. Payment instruments will be received subject to collection.

The transfer to the Optionee on the records of the Company or of the transfer agent of the Option Shares will be contingent upon (i) the Company’s receipt from the Optionee of the full purchase price for the Option Shares, as set forth above, (ii) the fulfillment of any other requirements contained herein or in the Plan or in any other agreement or provision of laws, and (iii) the receipt by the Company of any agreement, statement or other evidence that the Company may require to satisfy itself that the issuance of Stock to be purchased pursuant to the exercise of Stock Options under the Plan and any subsequent resale of the shares of Stock will be in compliance with applicable laws and regulations. In the event the Optionee chooses to pay the purchase price by previously-owned shares of Stock through the attestation method, the number of shares of Stock transferred to the Optionee upon the exercise of the Stock Option shall be net of the Shares attested to.

(b) The shares of Stock purchased upon exercise of this Stock Option shall be transferred to the Optionee on the records of the Company or of the transfer agent upon compliance to the satisfaction of the Administrator with all requirements under applicable laws or regulations in connection with such transfer and with the requirements hereof and of the Plan. The determination of the Administrator as to such compliance shall be final and binding on the Optionee. The Optionee shall not be deemed to be the holder of, or to have any of the rights of a holder with respect to, any shares of Stock subject to this Stock Option unless and until this Stock Option shall have been exercised pursuant to the terms hereof, the Company or the transfer agent shall have transferred the shares to the Optionee, and the Optionee’s name shall have been entered as the stockholder of record on the books of the Company. Thereupon, the Optionee shall have full voting, dividend and other ownership rights with respect to such shares of Stock.

(c) The minimum number of shares with respect to which this Stock Option may be exercised at any one time shall be 100 shares, unless the number of shares with respect to which this Stock Option is being exercised is the total number of shares subject to exercise under this Stock Option at the time.

(d) Notwithstanding any other provision hereof or of the Plan, no portion of this Stock Option shall be exercisable after the Expiration Date hereof.

3. Termination of Service Relationship. If the Optionee ceases to maintain a Service Relationship with the Company or a Subsidiary, the period within which to exercise the Stock Option may be subject to earlier termination as set forth below.

(a) Termination Due to Death. If the Optionee's Service Relationship with the Company or a Subsidiary terminates by reason of the Optionee's death, any portion of this Stock Option outstanding on the date of death may thereafter be exercised by the Optionee's legal representative or legatee for a period of 12 months from the date of death or until the Expiration Date, if earlier.

(b) Termination Due to Disability. If the Optionee's Service Relationship with the Company or a Subsidiary terminates by reason of the Optionee's disability (as determined by the Administrator), any portion of this Stock Option outstanding on the date on which the Optionee is determined to have a disability may thereafter be exercised by the Optionee for a period of 12 months from such date of disability or until the Expiration Date, if earlier.

(c) Other Termination. If the Optionee ceases to have a Service Relationship with the Company or a Subsidiary for any reason other than the Optionee's death or disability, any portion of this Stock Option outstanding on the date on which the Optionee's Service Relationship with the Company or a Subsidiary ceased may be exercised, to the extent exercisable on such date, for a period of three months from such date or until the Expiration Date, if earlier. Any portion of this Stock Option that is not exercisable on the date the Optionee's Service Relationship with the Company or a Subsidiary ceased shall terminate immediately and be of no further force or effect.

The Administrator's determination of the reason for termination of the Optionee's Service Relationship with the Company or a Subsidiary shall be conclusive and binding on the Optionee and his or her representatives or legatees.

4. Incorporation of Plan. Notwithstanding anything herein to the contrary, this Stock Option shall be subject to and governed by all the terms and conditions of the Plan, including the powers of the Administrator set forth in Section 2(b) of the Plan. Capitalized terms in this Agreement shall have the meaning specified in the Plan, unless a different meaning is specified herein.

5. Transferability. This Agreement is personal to the Optionee, is non-assignable and is not transferable in any manner, by operation of law or otherwise, other than by will or the laws of descent and distribution. This Stock Option is exercisable, during the Optionee's lifetime, only by the Optionee, and thereafter, only by the Optionee's legal representative or legatee.

6. No Obligation to Continue Service Relationship. Neither the Plan nor this Stock Option confers upon the Optionee any rights with respect to the continuation of Optionee's service as a Consultant or other Service Relationship with the Company or a Subsidiary.



7. Integration. This Agreement constitutes the entire agreement between the parties with respect to this Stock Option and supersedes all prior agreements and discussions between the parties concerning such subject matter.

8. Data Privacy Consent. In order to administer the Plan and this Agreement and to implement or structure future equity grants, the Company, its subsidiaries and affiliates and certain agents thereof (together, the “**Relevant Companies**”) may process any and all personal or professional data, including but not limited to Social Security or other identification number, home address and telephone number, date of birth and other information that is necessary or desirable for the administration of the Plan and/or this Agreement (the “**Relevant Information**”). By entering into this Agreement, the Optionee (i) authorizes the Company to collect, process, register and transfer to the Relevant Companies all Relevant Information; (ii) waives any privacy rights the Optionee may have with respect to the Relevant Information; (iii) authorizes the Relevant Companies to store and transmit such information in electronic form; and (iv) authorizes the transfer of the Relevant Information to any jurisdiction in which the Relevant Companies consider appropriate. The Optionee shall have access to, and the right to change, the Relevant Information. Relevant Information will only be used in accordance with applicable law.

9. Notices. Notices hereunder shall be mailed or delivered to the Company at its principal place of business and shall be mailed or delivered to the Optionee at the address on file with the Company or, in either case, at such other address as one party may subsequently furnish to the other party in writing.

**C4 THERAPEUTICS, INC.**

By: \_\_\_  
Title:

The foregoing Agreement is hereby accepted and the terms and conditions thereof hereby agreed to by the undersigned. Electronic acceptance of this Agreement pursuant to the Company’s instructions to the Optionee (including through an online acceptance process) is acceptable.

Dated: \_\_\_ \_\_\_

Optionee’s Signature

Optionee’s name and address:

\_\_\_  
\_\_\_  
\_\_\_

**NON-QUALIFIED STOCK OPTION AGREEMENT  
FOR NON-EMPLOYEE DIRECTORS  
UNDER THE C4 THERAPEUTICS, INC.  
2020 STOCK OPTION AND INCENTIVE PLAN**

Name of Optionee: \_\_\_\_

No. of Option Shares: \_\_\_\_

Option Exercise Price per Share: \$\_\_\_\_  
[FMV on Grant Date]

Grant Date: \_\_\_\_

Expiration Date: \_\_\_\_  
[No more than 10 years]

Pursuant to the C4 Therapeutics, Inc. 2020 Stock Option and Incentive Plan as amended through the date hereof (the “**Plan**”), C4 Therapeutics, Inc. (the “**Company**”) hereby grants to the Optionee named above, who is a Director of the Company but is not an employee of the Company, an option (the “**Stock Option**”) to purchase on or prior to the Expiration Date specified above all or part of the number of shares of Common Stock, par value \$0.0001 per share (the “**Stock**”), of the Company specified above at the Option Exercise Price per Share specified above subject to the terms and conditions set forth herein and in the Plan. This Stock Option is not intended to be an “incentive stock option” under Section 422 of the Internal Revenue Code of 1986, as amended.

1. Exercisability Schedule. No portion of this Stock Option may be exercised until such portion shall have become exercisable. Except as set forth below, and subject to the discretion of the Administrator (as defined in Section 2 of the Plan) to accelerate the exercisability schedule hereunder, this Stock Option shall be exercisable with respect to the following number of Option Shares on the dates indicated so long as the Optionee maintains a Service Relationship with the Company or a Subsidiary on each such date:

<u>Incremental Number of Option Shares Exercisable</u>	<u>Exercisability Date</u>
_____ ( ____%)	_____
_____ ( ____%)	_____
_____ ( ____%)	_____
_____ ( ____%)	_____
_____ ( ____%)	_____

However, notwithstanding anything to the contrary, one hundred percent (100%) of the Option Shares shall immediately become exercisable upon the termination of the Optionee’s Service Relationship due to the Optionee’s death or disability (as determined by the Administrator).

Once exercisable, this Stock Option shall continue to be exercisable at any time or times prior to the close of business on the Expiration Date, subject to the provisions hereof and of the Plan.

2. Manner of Exercise.

(a) The Optionee may exercise this Stock Option only in the following manner: from time to time on or prior to the Expiration Date of this Stock Option, the Optionee may give written notice to the Administrator of his or her election to purchase some or all of the Option Shares purchasable at the time of such notice. This notice shall specify the number of Option Shares to be purchased.

Payment of the purchase price for the Option Shares may be made by one or more of the following methods: (i) in cash, by certified or bank check or other instrument acceptable to the Administrator; (ii) through the delivery (or attestation to the ownership) of shares of Stock that have been purchased by the Optionee on the open market or that are beneficially owned by the Optionee and are not then subject to any restrictions under any Company plan and that otherwise satisfy any holding periods as may be required by the Administrator; (iii) by the Optionee delivering to the Company a properly executed exercise notice together with irrevocable instructions to a broker to promptly deliver to the Company cash or a check payable and acceptable to the Company to pay the option purchase price, *provided* that in the event the Optionee chooses to pay the option purchase price as so provided, the Optionee and the broker shall comply with such procedures and enter into such agreements of indemnity and other agreements as the Administrator shall prescribe as a condition of such payment procedure; (iv) by a “net exercise” arrangement pursuant to which the Company will reduce the number of shares of Stock issuable upon exercise by the largest whole number of shares with a Fair Market Value that does not exceed the aggregate exercise price; or (v) a combination of (i), (ii), (iii) and (iv) above. Payment instruments will be received subject to collection.

The transfer to the Optionee on the records of the Company or of the transfer agent of the Option Shares will be contingent upon (i) the Company’s receipt from the Optionee of the full purchase price for the Option Shares, as set forth above, (ii) the fulfillment of any other requirements contained herein or in the Plan or in any other agreement or provision of laws, and (iii) the receipt by the Company of any agreement, statement or other evidence that the Company may require to satisfy itself that the issuance of Stock to be purchased pursuant to the exercise of Stock Options under the Plan and any subsequent resale of the shares of Stock will be in compliance with applicable laws and regulations. In the event the Optionee chooses to pay the purchase price by previously-owned shares of Stock through the attestation method, the number of shares of Stock transferred to the Optionee upon the exercise of the Stock Option shall be net of the Shares attested to.

(b) The shares of Stock purchased upon exercise of this Stock Option shall be transferred to the Optionee on the records of the Company or of the transfer agent upon compliance to the satisfaction of the Administrator with all requirements under applicable laws or regulations in connection with such transfer and with the requirements hereof and of the Plan. The determination of the Administrator as to such compliance shall be final and binding on the Optionee. The Optionee shall not be deemed to be the holder of, or to have any of the rights of a holder with respect to, any shares of Stock subject to this Stock Option unless and until this Stock Option shall have been exercised pursuant to the terms hereof, the Company or the transfer agent shall have transferred the shares to the Optionee, and the Optionee’s name shall have been entered as the stockholder of record on the books of the Company. Thereupon, the Optionee shall have full voting, dividend and other ownership rights with respect to such shares of Stock.

(c) The minimum number of shares with respect to which this Stock Option may be exercised at any one time shall be 100 shares, unless the number of shares with respect to which this Stock Option is being exercised is the total number of shares subject to exercise under this Stock Option at the time.

(d) Notwithstanding any other provision hereof or of the Plan, no portion of this Stock Option shall be exercisable after the Expiration Date hereof.

3. Termination of Service Relationship. If the Optionee ceases to maintain a Service Relationship with the Company or a Subsidiary, the period within which to exercise the Stock Option may be subject to earlier termination as set forth below.

(a) Termination Due to Death. If the Optionee's Service Relationship with the Company or a Subsidiary terminates by reason of the Optionee's death, any portion of this Stock Option outstanding on such date may thereafter be exercised by the Optionee's legal representative or legatee for a period of 12 months from such date of death or until the Expiration Date, if earlier.

(b) Termination Due to Disability. If the Optionee's Service Relationship with the Company or a Subsidiary terminates by reason of the Optionee's disability (as determined by the Administrator), any portion of this Stock Option outstanding on the date on which the Optionee is determined to have a disability may thereafter be exercised by the Optionee for a period of 12 months from such date of disability or until the Expiration Date, if earlier.

(c) Other Termination. If the Optionee's Service Relationship with the Company or a Subsidiary terminates for any reason other than the Optionee's death or disability, any portion of this Stock Option outstanding on such date may be exercised, to the extent exercisable on the date the Optionee ceased to maintain a Service Relationship with the Company or a Subsidiary, for a period of six months from the date the Optionee's Service Relationship with the Company or a Subsidiary ceased or until the Expiration Date, if earlier. Any portion of this Stock Option that is not exercisable on the date the Optionee's Service Relationship with the Company or a Subsidiary ceases shall terminate immediately and be of no further force or effect.

The Administrator's determination of the reason for termination of the Optionee's Service Relationship with the Company or a Subsidiary shall be conclusive and binding on the Optionee and his or her representatives or legatees.

4. Incorporation of Plan. Notwithstanding anything herein to the contrary, this Stock Option shall be subject to and governed by all the terms and conditions of the Plan, including the powers of the Administrator set forth in Section 2(b) of the Plan. Capitalized terms in this Agreement shall have the meaning specified in the Plan, unless a different meaning is specified herein.

5. Transferability. This Agreement is personal to the Optionee, is non-assignable and is not transferable in any manner, by operation of law or otherwise, other than by will or the laws of descent and distribution. This Stock Option is exercisable, during the Optionee's lifetime, only by the Optionee, and thereafter, only by the Optionee's legal representative or legatee.

6. No Obligation to Continue Service Relationship. Neither the Plan nor this Stock Option confers upon the Optionee any rights with respect to the continuation of the Optionee's service as a Director or any other Service Relationship with the Company or a Subsidiary.

7. Integration. This Agreement constitutes the entire agreement between the parties with respect to this Stock Option and supersedes all prior agreements and discussions between the parties concerning such subject matter.

8. Data Privacy Consent. In order to administer the Plan and this Agreement and to implement or structure future equity grants, the Company, its subsidiaries and affiliates and certain agents thereof (together, the “**Relevant Companies**”) may process any and all personal or professional data, including but not limited to Social Security or other identification number, home address and telephone number, date of birth and other information that is necessary or desirable for the administration of the Plan and/or this Agreement (the “**Relevant Information**”). By entering into this Agreement, the Optionee (i) authorizes the Company to collect, process, register and transfer to the Relevant Companies all Relevant Information; (ii) waives any privacy rights the Optionee may have with respect to the Relevant Information; (iii) authorizes the Relevant Companies to store and transmit such information in electronic form; and (iv) authorizes the transfer of the Relevant Information to any jurisdiction in which the Relevant Companies consider appropriate. The Optionee shall have access to, and the right to change, the Relevant Information. Relevant Information will only be used in accordance with applicable law.

9. Notices. Notices hereunder shall be mailed or delivered to the Company at its principal place of business and shall be mailed or delivered to the Optionee at the address on file with the Company or, in either case, at such other address as one party may subsequently furnish to the other party in writing.

**C4 THERAPEUTICS, INC.**

By: \_\_\_\_\_  
Title:

The foregoing Agreement is hereby accepted and the terms and conditions thereof hereby agreed to by the undersigned. Electronic acceptance of this Agreement pursuant to the Company’s instructions to the Optionee (including through an online acceptance process) is acceptable.

Dated:    —   —

Optionee’s Signature

Optionee’s name and address:

—  
—  
—

**NON-QUALIFIED STOCK OPTION AGREEMENT  
FOR COMPANY EMPLOYEES  
UNDER THE C4 THERAPEUTICS, INC.  
2020 STOCK OPTION AND INCENTIVE PLAN**

Name of Optionee: \_\_\_\_

No. of Option Shares: \_\_\_\_

Option Exercise Price per Share: \$\_\_\_\_  
[FMV on Grant Date]

Grant Date: \_\_\_\_

Expiration Date: \_\_\_\_

Pursuant to the C4 Therapeutics, Inc. 2020 Stock Option and Incentive Plan as amended through the date hereof (the “**Plan**”), C4 Therapeutics, Inc. (the “**Company**”) hereby grants to the Optionee named above an option (the “**Stock Option**”) to purchase on or prior to the Expiration Date specified above all or part of the number of shares of Common Stock, par value \$0.0001 per share (the “**Stock**”), of the Company specified above at the Option Exercise Price per Share specified above subject to the terms and conditions set forth herein and in the Plan. This Stock Option is not intended to be an “incentive stock option” under Section 422 of the Internal Revenue Code of 1986, as amended.

1. Exercisability Schedule. No portion of this Stock Option may be exercised until such portion shall have become exercisable. Except as set forth below, and subject to the discretion of the Administrator (as defined in Section 2 of the Plan) to accelerate the exercisability schedule hereunder, this Stock Option shall be exercisable with respect to the following number of Option Shares on the dates indicated so long as the Optionee maintains a Service Relationship with the Company or a Subsidiary on each such date:

<u>Incremental Number of Option Shares Exercisable</u>	<u>Exercisability Date</u>
_____ ( ____ %)	_____
_____ ( ____ %)	_____
_____ ( ____ %)	_____
_____ ( ____ %)	_____
_____ ( ____ %)	_____

However, notwithstanding anything to the contrary, one hundred percent (100%) of the Option Shares shall immediately become exercisable upon the termination of the Optionee’s Service Relationship due to the Optionee’s death or disability (as determined by the Administrator).

Once exercisable, this Stock Option shall continue to be exercisable at any time or times prior to the close of business on the Expiration Date, subject to the provisions hereof and of the Plan.

2. Manner of Exercise.

(a) The Optionee may exercise this Stock Option only in the following manner: from time to time on or prior to the Expiration Date of this Stock Option, the Optionee may give written notice to the Administrator of his or her election to purchase some or all of the Option Shares purchasable at the time of such notice. This notice shall specify the number of Option Shares to be purchased.

Payment of the purchase price for the Option Shares may be made by one or more of the following methods: (i) in cash, by certified or bank check or other instrument acceptable to the Administrator; (ii) through the delivery (or attestation to the ownership) of shares of Stock that have been purchased by the Optionee on the open market or that are beneficially owned by the Optionee and are not then subject to any restrictions under any Company plan and that otherwise satisfy any holding periods as may be required by the Administrator; (iii) by the Optionee delivering to the Company a properly executed exercise notice together with irrevocable instructions to a broker to promptly deliver to the Company cash or a check payable and acceptable to the Company to pay the option purchase price, *provided* that in the event the Optionee chooses to pay the option purchase price as so provided, the Optionee and the broker shall comply with such procedures and enter into such agreements of indemnity and other agreements as the Administrator shall prescribe as a condition of such payment procedure; (iv) by a “net exercise” arrangement pursuant to which the Company will reduce the number of shares of Stock issuable upon exercise by the largest whole number of shares with a Fair Market Value that does not exceed the aggregate exercise price; or (v) a combination of (i), (ii), (iii) and (iv) above. Payment instruments will be received subject to collection.

The transfer to the Optionee on the records of the Company or of the transfer agent of the Option Shares will be contingent upon (i) the Company’s receipt from the Optionee of the full purchase price for the Option Shares, as set forth above, (ii) the fulfillment of any other requirements contained herein or in the Plan or in any other agreement or provision of laws, and (iii) the receipt by the Company of any agreement, statement or other evidence that the Company may require to satisfy itself that the issuance of Stock to be purchased pursuant to the exercise of Stock Options under the Plan and any subsequent resale of the shares of Stock will be in compliance with applicable laws and regulations. In the event the Optionee chooses to pay the purchase price by previously-owned shares of Stock through the attestation method, the number of shares of Stock transferred to the Optionee upon the exercise of the Stock Option shall be net of the Shares attested to.

(b) The shares of Stock purchased upon exercise of this Stock Option shall be transferred to the Optionee on the records of the Company or of the transfer agent upon compliance to the satisfaction of the Administrator with all requirements under applicable laws or regulations in connection with such transfer and with the requirements hereof and of the Plan. The determination of the Administrator as to such compliance shall be final and binding on the Optionee. The Optionee shall not be deemed to be the holder of, or to have any of the rights of a holder with respect to, any shares of Stock subject to this Stock Option unless and until this Stock Option shall have been exercised pursuant to the terms hereof, the Company or the transfer agent shall have transferred the shares to the Optionee, and the Optionee’s name shall have been entered as the stockholder of record on the books of the Company. Thereupon, the Optionee shall have full voting, dividend and other ownership rights with respect to such shares of Stock.

(c) The minimum number of shares with respect to which this Stock Option may be exercised at any one time shall be 100 shares, unless the number of shares with respect to which this Stock Option is being exercised is the total number of shares subject to exercise under this Stock Option at the time.

(d) Notwithstanding any other provision hereof or of the Plan, no portion of this Stock Option shall be exercisable after the Expiration Date hereof.

3. Termination of Service Relationship. If the Optionee's employment by or other Service Relationship with the Company or a Subsidiary is terminated, the period within which to exercise the Stock Option may be subject to earlier termination as set forth below.

(a) Termination Due to Death. If the Optionee's employment or other Service Relationship with the Company or a Subsidiary terminates by reason of the Optionee's death, any portion of this Stock Option outstanding on the date of death may thereafter be exercised by the Optionee's legal representative or legatee for a period of 12 months from the date of death or until the Expiration Date, if earlier.

(b) Termination Due to Disability. If the Optionee's employment or other Service Relationship with the Company or a Subsidiary terminates by reason of the Optionee's disability (as determined by the Administrator), any portion of this Stock Option outstanding on the date on which the Optionee is determined to have a disability may thereafter be exercised by the Optionee for a period of 12 months from such date of disability or until the Expiration Date, if earlier.

(c) Termination for Cause. If the Optionee's employment or other Service Relationship with the Company or a Subsidiary terminates for Cause, any portion of this Stock Option outstanding on such date shall terminate immediately and be of no further force and effect. For purposes hereof, "**Cause**" shall mean, unless otherwise provided in an employment agreement between the Company and the Optionee, a determination by the Administrator that the Optionee shall be dismissed as a result of (i) any material breach by the Optionee of any agreement between the Optionee and the Company; (ii) the conviction of, indictment for or plea of nolo contendere by the Optionee to a felony or a crime involving moral turpitude; or (iii) any material misconduct or willful and deliberate non-performance (other than by reason of disability) by the Optionee of the Optionee's duties to the Company.

(d) Other Termination. If the Optionee's employment or other Service Relationship with the Company or a Subsidiary terminates for any reason other than the Optionee's death, disability or Cause, and unless otherwise determined by the Administrator, any portion of this Stock Option outstanding on the date on which the Optionee's employment or other Service Relationship with the Company or a Subsidiary terminated may be exercised, to the extent exercisable on such date, for a period of three months from such date of termination or until the Expiration Date, if earlier. Any portion of this Stock Option that is not exercisable on the date of termination shall terminate immediately and be of no further force or effect.

The Administrator's determination of the reason for termination of the Optionee's employment or other Service Relationship with the Company or a Subsidiary shall be conclusive and binding on the Optionee and his or her representatives or legatees.

4. Incorporation of Plan. Notwithstanding anything herein to the contrary, this Stock Option shall be subject to and governed by all the terms and conditions of the Plan, including the powers of the Administrator set forth in Section 2(b) of the Plan. Capitalized terms in this Agreement shall have the meaning specified in the Plan, unless a different meaning is specified herein.

5. Transferability. This Agreement is personal to the Optionee, is non-assignable and is not transferable in any manner, by operation of law or otherwise, other than by will or the laws of descent and distribution. This Stock Option is exercisable, during the Optionee's



lifetime, only by the Optionee, and thereafter, only by the Optionee's legal representative or legatee.

6. Tax Withholding. The Optionee shall, not later than the date as of which the exercise of this Stock Option becomes a taxable event for Federal income tax purposes, pay to the Company or make arrangements satisfactory to the Administrator for payment of any Federal, state, and local taxes required by law to be withheld on account of such taxable event. The Company shall have the authority to cause the required tax withholding obligation to be satisfied, in whole or in part, by withholding from shares of Stock to be issued to the Optionee a number of shares of Stock with an aggregate Fair Market Value that would satisfy the withholding amount due.

7. No Obligation to Continue Service Relationship. Neither the Company nor any Subsidiary is obligated by or as a result of the Plan or this Agreement to continue the Optionee in employment or other Service Relationship with the Company or a Subsidiary and neither the Plan nor this Agreement shall interfere in any way with the right of the Company or any Subsidiary to terminate the Optionee's employment or other Service Relationship with the Company or a Subsidiary at any time.

8. Integration. This Agreement constitutes the entire agreement between the parties with respect to this Stock Option and supersedes all prior agreements and discussions between the parties concerning such subject matter.

9. Data Privacy Consent. In order to administer the Plan and this Agreement and to implement or structure future equity grants, the Company, its subsidiaries and affiliates and certain agents thereof (together, the "**Relevant Companies**") may process any and all personal or professional data, including but not limited to Social Security or other identification number, home address and telephone number, date of birth and other information that is necessary or desirable for the administration of the Plan and/or this Agreement (the "**Relevant Information**"). By entering into this Agreement, the Optionee (i) authorizes the Company to collect, process, register and transfer to the Relevant Companies all Relevant Information; (ii) waives any privacy rights the Optionee may have with respect to the Relevant Information; (iii) authorizes the Relevant Companies to store and transmit such information in electronic form; and (iv) authorizes the transfer of the Relevant Information to any jurisdiction in which the Relevant Companies consider appropriate. The Optionee shall have access to, and the right to change, the Relevant Information. Relevant Information will only be used in accordance with applicable law.

10. Notices. Notices hereunder shall be mailed or delivered to the Company at its principal place of business and shall be mailed or delivered to the Optionee at the address on file

with the Company or, in either case, at such other address as one party may subsequently furnish to the other party in writing.

**C4 THERAPEUTICS, INC.**

By: \_\_\_  
Title:

The foregoing Agreement is hereby accepted and the terms and conditions thereof hereby agreed to by the undersigned. Electronic acceptance of this Agreement pursuant to the Company's instructions to the Optionee (including through an online acceptance process) is acceptable.

Dated: \_\_\_ \_\_\_

Optionee's Signature

Optionee's name and address:

\_\_\_  
\_\_\_  
\_\_\_

**RESTRICTED STOCK AWARD AGREEMENT  
UNDER THE C4 THERAPEUTICS, INC.  
2020 STOCK OPTION AND INCENTIVE PLAN**

Name of Grantee: \_\_\_

No. of Shares: \_\_\_

Grant Date: \_\_\_

Pursuant to the C4 Therapeutics, Inc. 2020 Stock Option and Incentive Plan (the “**Plan**”) as amended through the date hereof, C4 Therapeutics, Inc. (the “**Company**”) hereby grants a Restricted Stock Award (an “**Award**”) to the Grantee named above. Upon acceptance of this Award, the Grantee shall receive the number of shares of Common Stock, par value \$0.0001 per share (the “**Stock**”) of the Company specified above, subject to the restrictions and conditions set forth herein and in the Plan. The Company acknowledges the receipt from the Grantee of consideration with respect to the par value of the Stock in the form of cash, past or future services rendered to the Company by the Grantee or such other form of consideration as is acceptable to the Administrator.

1. Award. The shares of Restricted Stock awarded hereunder shall be issued and held by the Company’s transfer agent in book entry form, and the Grantee’s name shall be entered as the stockholder of record on the books of the Company. Thereupon, the Grantee shall have all the rights of a stockholder with respect to such shares, including voting and dividend rights, subject, however, to the restrictions and conditions specified in Paragraph 2 below. The Grantee shall (i) sign and deliver to the Company a copy of this Award Agreement and (ii) deliver to the Company a stock power endorsed in blank.

2. Restrictions and Conditions.

(a) Any book entries for the shares of Restricted Stock granted herein shall bear an appropriate legend, as determined by the Administrator in its sole discretion, to the effect that such shares are subject to restrictions as set forth herein and in the Plan.

(b) Shares of Restricted Stock granted herein may not be sold, assigned, transferred, pledged or otherwise encumbered or disposed of by the Grantee prior to vesting.

(c) If the Grantee’s employment with the Company and its Subsidiaries is voluntarily or involuntarily terminated for any reason prior to vesting of shares of Restricted Stock granted herein, all shares of Restricted Stock shall immediately and automatically be forfeited and returned to the Company.

3. Vesting of Restricted Stock. The restrictions and conditions in Paragraph 2 of this Agreement shall lapse on the vesting date or dates specified in the following schedule (each, a “**Vesting Date**” and, collectively, the “**Vesting Dates**”) so long as the Grantee maintains a Service Relationship on each such date. If a series of Vesting Dates is specified, then the restrictions and conditions in Paragraph 2 shall lapse only with respect to the number of shares of Restricted Stock specified as vested on each such date.

<u>Incremental Number of Shares Vested</u>	<u>Vesting Date</u>
_____ ( ___ %)	_____
_____ ( ___ %)	_____
_____ ( ___ %)	_____
_____ ( ___ %)	_____
_____ ( ___ %)	_____

However, notwithstanding anything to the contrary, one hundred percent (100%) of the Shares shall become immediately vested upon the termination of the Grantee's Service Relationship due to the Grantee's death or disability (as determined by the Administrator).

Subsequent to such Vesting Date(s), the shares of Stock on which all restrictions and conditions have lapsed shall no longer be deemed Restricted Stock.

4. Dividends. Dividends on shares of Restricted Stock shall be paid currently to the Grantee.

5. Incorporation of Plan. Notwithstanding anything herein to the contrary, this Award shall be subject to and governed by all the terms and conditions of the Plan, including the powers of the Administrator set forth in Section 2(b) of the Plan. Capitalized terms in this Agreement shall have the meaning specified in the Plan, unless a different meaning is specified herein.

6. Transferability. This Agreement is personal to the Grantee, is non-assignable and is not transferable in any manner, by operation of law or otherwise, other than by will or the laws of descent and distribution.

7. Tax Withholding. The Grantee shall, not later than the date as of which the receipt of this Award becomes a taxable event for Federal income tax purposes, pay to the Company or make arrangements satisfactory to the Administrator for payment of any Federal, state, and local taxes required by law to be withheld on account of such taxable event. Except in the case where an election is made pursuant to Paragraph 8 below, the Company shall have the authority to cause the required tax withholding obligation to be satisfied, in whole or in part, by either withholding from shares of Stock to be issued to the Grantee a number of shares of Stock with an aggregate Fair Market Value that would satisfy the withholding amount due or selling from the number of shares of Stock to be issued to the Grantee, the number of shares of Stock necessary to satisfy the Federal, state and local taxes required by law to be withheld from the Grantee on account of such transfer.

8. Election Under Section 83(b). The Grantee and the Company hereby agree that the Grantee may, within 30 days following the Grant Date of this Award, file with the Internal Revenue Service and the Company an election under Section 83(b) of the Internal Revenue Code. In the event the Grantee makes such an election, he or she agrees to provide a copy of the election to the Company. The Grantee acknowledges that he or she is responsible for obtaining the advice of his or her tax advisors with regard to the Section 83(b) election and that he or she is relying solely on such advisors and not on any statements or representations of the Company or any of its agents with regard to such election.

9. No Obligation to Continue Service Relationship. Neither the Company nor any Subsidiary is obligated by or as a result of the Plan or this Agreement to continue the Grantee in employment or any other Service Relationship with the Company or a Subsidiary and neither the Plan nor this Agreement shall interfere in any way with the right of the Company or any Subsidiary to terminate the Grantee's employment or other Service Relationship with the Company or a Subsidiary at any time.

10. Integration. This Agreement constitutes the entire agreement between the parties with respect to this Award and supersedes all prior agreements and discussions between the parties concerning such subject matter.

11. Data Privacy Consent. In order to administer the Plan and this Agreement and to implement or structure future equity grants, the Company, its subsidiaries and affiliates and certain agents thereof (together, the "**Relevant Companies**") may process any and all personal or professional data, including but not limited to Social Security or other identification number, home address and telephone number, date of birth and other information that is necessary or desirable for the administration of the Plan and/or this Agreement (the "**Relevant Information**"). By entering into this Agreement, the Grantee (i) authorizes the Company to collect, process, register and transfer to the Relevant Companies all Relevant Information; (ii) waives any privacy rights the Grantee may have with respect to the Relevant Information; (iii) authorizes the Relevant Companies to store and transmit such information in electronic form; and (iv) authorizes the transfer of the Relevant Information to any jurisdiction in which the Relevant Companies consider appropriate. The Grantee shall have access to, and the right to change, the Relevant Information. Relevant Information will only be used in accordance with applicable law.

12. Notices. Notices hereunder shall be mailed or delivered to the Company at its principal place of business and shall be mailed or delivered to the Grantee at the address on file with the Company or, in either case, at such other address as one party may subsequently furnish to the other party in writing.

**C4 THERAPEUTICS, INC.**

By: \_\_\_\_\_  
Title: \_\_\_\_\_

The foregoing Agreement is hereby accepted and the terms and conditions thereof hereby agreed to by the undersigned. Electronic acceptance of this Agreement pursuant to the Company's instructions to the Grantee (including through an online acceptance process) is acceptable.

Dated: \_\_\_\_ \_\_\_\_

Grantee's Signature

Grantee's name and address:

\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

**RESTRICTED STOCK UNIT AWARD AGREEMENT  
FOR NON-EMPLOYEE DIRECTORS  
UNDER THE C4 THERAPEUTICS, INC.  
2020 STOCK OPTION AND INCENTIVE PLAN**

Name of Grantee: \_\_\_\_

No. of Restricted Stock Units: \_\_\_\_

Grant Date: \_\_\_\_

Pursuant to the C4 Therapeutics, Inc. 2020 Stock Option and Incentive Plan as amended through the date hereof (the “**Plan**”), C4 Therapeutics, Inc. (the “**Company**”) hereby grants an award of the number of Restricted Stock Units listed above (an “**Award**”) to the Grantee named above. Each Restricted Stock Unit shall relate to one share of Common Stock, par value \$0.0001 per share (the “**Stock**”) of the Company.

1. Restrictions on Transfer of Award. This Award may not be sold, transferred, pledged, assigned or otherwise encumbered or disposed of by the Grantee, and any shares of Stock issuable with respect to the Award may not be sold, transferred, pledged, assigned or otherwise encumbered or disposed of until (i) the Restricted Stock Units have vested as provided in Paragraph 2 of this Agreement and (ii) shares of Stock have been issued to the Grantee in accordance with the terms of the Plan and this Agreement.

2. Vesting of Restricted Stock Units. The restrictions and conditions of Paragraph 1 of this Agreement shall lapse on the vesting date or dates specified in the following schedule (each a “**Vesting Date**” and, collectively, the “**Vesting Dates**”) so long as the Grantee maintains a Service Relationship with the Company or a Subsidiary on each such Vesting Date. If a series of Vesting Dates is specified, then the restrictions and conditions in Paragraph 1 shall lapse only with respect to the number of Restricted Stock Units specified as vested on each such date.

<u>Incremental Number of Restricted Stock Units Vested</u>	<u>Vesting Date</u>
_____ ( ____ %)	_____
_____ ( ____ %)	_____
_____ ( ____ %)	_____
_____ ( ____ %)	_____

However, notwithstanding anything to the contrary, one hundred percent (100%) of the Restricted Stock Units shall become immediately vested upon the termination of the Grantee’s Service Relationship due to the Grantee’s death or disability (as determined by the Administrator).

3. Termination of Service Relationship. If the Grantee’s Service Relationship with the Company and its Subsidiaries terminates for any reason prior to the satisfaction of the vesting conditions set forth in Paragraph 2 above, any Restricted Stock Units that have not vested as of such date shall automatically and without notice terminate and be forfeited, and neither the Grantee nor any of his or her successors, heirs, assigns, or personal representatives will thereafter have any further rights or interests in such unvested Restricted Stock Units.

4. Issuance of Shares of Stock. As soon as practicable following each Vesting Date (but in no event later than two and one-half months after the end of the year in which the Vesting Date occurs), the Company shall issue to the Grantee the number of shares of Stock equal to the aggregate number of Restricted Stock Units that have vested pursuant to Paragraph 2 of this Agreement on such date and the Grantee shall thereafter have all the rights of a stockholder of the Company with respect to such shares.

5. Incorporation of Plan. Notwithstanding anything herein to the contrary, this Agreement shall be subject to and governed by all the terms and conditions of the Plan, including the powers of the Administrator set forth in Section 2(b) of the Plan. Capitalized terms in this Agreement shall have the meaning specified in the Plan, unless a different meaning is specified herein.

6. Section 409A of the Code. This Agreement shall be interpreted in such a manner that all provisions relating to the settlement of the Award are exempt from the requirements of Section 409A of the Code as “short-term deferrals” as described in Section 409A of the Code.

7. No Obligation to Continue Service Relationship. Neither the Plan nor this Award confers upon the Grantee any rights with respect to the continuation of the Grantee’s service as a Director or any other Service Relationship with the Company or a Subsidiary.

8. Integration. This Agreement constitutes the entire agreement between the parties with respect to this Award and supersedes all prior agreements and discussions between the parties concerning such subject matter.

9. Data Privacy Consent. In order to administer the Plan and this Agreement and to implement or structure future equity grants, the Company, its subsidiaries and affiliates and certain agents thereof (together, the “**Relevant Companies**”) may process any and all personal or professional data, including but not limited to Social Security or other identification number, home address and telephone number, date of birth and other information that is necessary or desirable for the administration of the Plan and/or this Agreement (the “**Relevant Information**”). By entering into this Agreement, the Grantee (i) authorizes the Company to collect, process, register and transfer to the Relevant Companies all Relevant Information; (ii) waives any privacy rights the Grantee may have with respect to the Relevant Information; (iii) authorizes the Relevant Companies to store and transmit such information in electronic form; and (iv) authorizes the transfer of the Relevant Information to any jurisdiction in which the Relevant Companies consider appropriate. The Grantee shall have access to, and the right to change, the Relevant Information. Relevant Information will only be used in accordance with applicable law.

10. Notices. Notices hereunder shall be mailed or delivered to the Company at its principal place of business and shall be mailed or delivered to the Grantee at the address on file



with the Company or, in either case, at such other address as one party may subsequently furnish to the other party in writing.

**C4 THERAPEUTICS, INC.**

By: \_\_\_  
Title:

The foregoing Agreement is hereby accepted and the terms and conditions thereof hereby agreed to by the undersigned. Electronic acceptance of this Agreement pursuant to the Company's instructions to the Grantee (including through an online acceptance process) is acceptable.

Dated: \_\_\_ \_\_\_

Grantee's Signature

Grantee's name and address:

\_\_\_  
\_\_\_  
\_\_\_

**RESTRICTED STOCK UNIT AWARD AGREEMENT  
FOR COMPANY EMPLOYEES  
UNDER THE C4 THERAPEUTICS, INC.  
2020 STOCK OPTION AND INCENTIVE PLAN**

Name of Grantee: \_\_\_\_

No. of Restricted Stock Units: \_\_\_\_

Grant Date: \_\_\_\_

Pursuant to the C4 Therapeutics, Inc. 2020 Stock Option and Incentive Plan as amended through the date hereof (the “**Plan**”), C4 Therapeutics, Inc. (the “**Company**”) hereby grants an award of the number of Restricted Stock Units listed above (an “**Award**”) to the Grantee named above. Each Restricted Stock Unit shall relate to one share of Common Stock, par value \$0.0001 per share (the “**Stock**”) of the Company.

1. Restrictions on Transfer of Award. This Award may not be sold, transferred, pledged, assigned or otherwise encumbered or disposed of by the Grantee, and any shares of Stock issuable with respect to the Award may not be sold, transferred, pledged, assigned or otherwise encumbered or disposed of until (i) the Restricted Stock Units have vested as provided in Paragraph 2 of this Agreement and (ii) shares of Stock have been issued to the Grantee in accordance with the terms of the Plan and this Agreement.

2. Vesting of Restricted Stock Units. The restrictions and conditions of Paragraph 1 of this Agreement shall lapse on the vesting date or dates specified in the following schedule (each a “**Vesting Date**” and, collectively, the “**Vesting Dates**”) so long as the Grantee maintains a Service Relationship with the Company or a Subsidiary on each such Vesting Date. If a series of Vesting Dates is specified, then the restrictions and conditions in Paragraph 1 shall lapse only with respect to the number of Restricted Stock Units specified as vested on each such date.

<u>Incremental Number of Restricted Stock Units Vested</u>	<u>Vesting Date</u>
_____ ( ____ %)	_____
_____ ( ____ %)	_____
_____ ( ____ %)	_____
_____ ( ____ %)	_____

However, notwithstanding anything to the contrary, one hundred percent (100%) of the Restricted Stock Units shall become immediately vested upon the termination of the Grantee’s Service Relationship due to the Grantee’s death or disability (as determined by the Administrator).

3. Termination of Service Relationship. If the Grantee’s employment or other Service Relationship with the Company and its Subsidiaries terminates for any reason prior to the satisfaction of the vesting conditions set forth in Paragraph 2 above, any Restricted Stock Units that have not vested as of such date shall automatically and without notice terminate and be forfeited, and neither the Grantee nor any of his or her successors, heirs, assigns, or personal

representatives will thereafter have any further rights or interests in such unvested Restricted Stock Units.

4. Issuance of Shares of Stock. As soon as practicable following each Vesting Date (but in no event later than two and one-half months after the end of the year in which the Vesting Date occurs), the Company shall issue to the Grantee the number of shares of Stock equal to the aggregate number of Restricted Stock Units that have vested pursuant to Paragraph 2 of this Agreement on such date and the Grantee shall thereafter have all the rights of a stockholder of the Company with respect to such shares.

5. Incorporation of Plan. Notwithstanding anything herein to the contrary, this Agreement shall be subject to and governed by all the terms and conditions of the Plan, including the powers of the Administrator set forth in Section 2(b) of the Plan. Capitalized terms in this Agreement shall have the meaning specified in the Plan, unless a different meaning is specified herein.

6. Tax Withholding. The Grantee shall, not later than the date as of which the receipt of this Award becomes a taxable event for Federal income tax purposes, pay to the Company or make arrangements satisfactory to the Administrator for payment of any Federal, state, and local taxes required by law to be withheld on account of such taxable event. The Company shall have the authority to cause the required tax withholding obligation to be satisfied, in whole or in part, by either withholding from shares of Stock to be issued to the Grantee a number of shares of Stock with an aggregate Fair Market Value that would satisfy the withholding amount due or selling from the number of shares of Stock to be issued to the Grantee, the number of shares of Stock necessary to satisfy the Federal, state and local taxes required by law to be withheld from the Grantee on account of such transfer.

7. Section 409A of the Code. This Agreement shall be interpreted in such a manner that all provisions relating to the settlement of the Award are exempt from the requirements of Section 409A of the Code as “short-term deferrals” as described in Section 409A of the Code.

8. No Obligation to Continue Service Relationship. Neither the Company nor any Subsidiary is obligated by or as a result of the Plan or this Agreement to continue the Grantee in employment or other Service Relationship with the Company or a Subsidiary, and neither the Plan nor this Agreement shall interfere in any way with the right of the Company or any Subsidiary to terminate the employment or other Service Relationship with the Company or a Subsidiary of the Grantee at any time.

9. Integration. This Agreement constitutes the entire agreement between the parties with respect to this Award and supersedes all prior agreements and discussions between the parties concerning such subject matter.

10. Data Privacy Consent. In order to administer the Plan and this Agreement and to implement or structure future equity grants, the Company, its subsidiaries and affiliates and certain agents thereof (together, the “**Relevant Companies**”) may process any and all personal or professional data, including but not limited to Social Security or other identification number, home address and telephone number, date of birth and other information that is necessary or desirable for the administration of the Plan and/or this Agreement (the “**Relevant Information**”). By entering into this Agreement, the Grantee (i) authorizes the Company to collect, process, register and transfer to the Relevant Companies all Relevant Information; (ii) waives any privacy rights the Grantee may have with respect to the Relevant Information; (iii) authorizes the Relevant Companies to store and transmit such information in electronic form; and (iv) authorizes the transfer of the Relevant Information to any jurisdiction in which the Relevant Companies consider appropriate. The Grantee shall have access to, and the right to change, the

Relevant Information. Relevant Information will only be used in accordance with applicable law.

11. Notices. Notices hereunder shall be mailed or delivered to the Company at its principal place of business and shall be mailed or delivered to the Grantee at the address on file with the Company or, in either case, at such other address as one party may subsequently furnish to the other party in writing.

**C4 THERAPEUTICS, INC.**

By: \_\_\_\_\_  
Title:

The foregoing Agreement is hereby accepted and the terms and conditions thereof hereby agreed to by the undersigned. Electronic acceptance of this Agreement pursuant to the Company's instructions to the Grantee (including through an online acceptance process) is acceptable.

Dated: \_\_\_\_

Grantee's Signature

Grantee's name and address:

\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

**SUBSIDIARIES**

**Subsidiary**

C4T Securities Corporation

**Jurisdiction of Incorporation**

Massachusetts

**Consent of Independent Registered Public Accounting Firm**

We consent to the incorporation by reference in the registration statements (No. 333-260972) on Form S-3 and (No. 333-249286, No. 333-254145, and No. 333-262949) on Form S-8 of our report dated February 23, 2023, with respect to the consolidated financial statements of C4 Therapeutics, Inc.

/s/ KPMG LLP

Boston, Massachusetts

February 23, 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, Andrew J. Hirsch, certify that:

1. I have reviewed this Annual Report on Form 10-K of C-4 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: February 23, 2023

By: \_\_\_\_\_ /s/ Andrew J. Hirsch

**Andrew J. Hirsch**  
**President and Chief Executive Officer**  
**(Principal executive officer)**

**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, Lauren A. White, certify that:

1. I have reviewed this Annual Report on Form 10-K of C-4 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: February 23, 2023

By: \_\_\_\_\_ /s/ Lauren A. White

**Lauren A. White**  
**Chief Financial Officer**  
**(Principal financial officer)**



**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 Quarterly Report of C4 Therapeutics (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: February 23, 2023

By: \_\_\_\_\_ /s/ Andrew J. Hirsch  
**Andrew J. Hirsch**  
**President and Chief Executive Officer**  
**(Principal executive officer)**

