CHIMERIX INC
Form 10-K
March 05, 2019

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

Form 10-K

(Mark One)
x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2018
or
o 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: 001-35867

Chimerix, Inc.
(Exact Name of Registrant as Specified in its Charter)

Delaware	33-0903395
(State or Other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification No.)
2505 Meridian Parkway, Suite 100 Durham, North Carolina	27713
(Address of Principal Executive Offices)	(Zip Code)

(919) 806-1074
(Registrant's Telephone Number, Including Area Code)
Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	Name of Each Exchange on Which Registered
Common Stock, par value $0.001 per share	The Nasdaq Stock Market LLC

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

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes o No x
Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes o No x

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 x No o

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 x No o

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of the registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. x

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 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 o	Accelerated filer x	
Non-accelerated filer o	Smaller reporting company x	
	Emerging growth company o	

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. o

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Securities Exchange Act of 1934). Yes o No x

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant based upon the closing price of its Common Stock on The Nasdaq Global Market on June 29, 2018 was $124,953,651.

The number of outstanding shares of the registrant's common stock, par value $0.001 per share, as of February 26, 2019 was 50,903,196.

DOCUMENTS INCORPORATED BY REFERENCE

Document Description	10-K Part
Portions of the registrant's notice of annual meeting of stockholders and proxy statement to be filed pursuant to Regulation 14A within 120 days after registrant's fiscal year end of December 31, 2018 are incorporated by reference into Part III of this report……	III

CHIMERIX, INC.
FORM 10-K
For the Fiscal Year Ended December 31, 2018
Table of Contents

		Page
PART I		
Item 1	Business	3
Item 1A	Risk Factors	21
Item 1B	Unresolved Staff Comments	49
Item 2	Properties	49
Item 3	Legal Proceedings	49
Item 4	Mine Safety Disclosures	49
PART II		
Item 5	Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities	50
Item 6	Selected Financial Data	51
Item 7	Management's Discussion and Analysis of Financial Condition and Results of Operations	52
Item 7A	Quantitative and Qualitative Disclosures About Market Risk	65
Item 8	Financial Statements and Supplementary Data	66
Item 9	Changes in and Disagreements With Accountants on Accounting and Financial Disclosure	91
Item 9A	Controls and Procedures	91
Item 9B	Other Information	92
PART III		
Item 10	Directors, Executive Officers and Corporate Governance	93
Item 11	Executive Compensation	93
Item 12	Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters	93
Item 13	Certain Relationships and Related Transactions, and Director Independence	93
Item 14	Principal Accounting Fees and Services	93
PART IV		
Item 15	Exhibits, Financial Statement Schedules	94
Signatures		

PART I

Forward-Looking Statements

This Annual Report on Form 10-K (Annual Report) may contain "forward-looking statements" within the meaning of the federal securities laws made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of various factors, including those set forth below under Part I, Item 1A, "Risk Factors" in this Annual Report. Except as required by law, we assume no obligation to update these forward-looking statements, whether as a result of new information, future events or otherwise. These statements, which represent our current expectations or beliefs concerning various future events that are subject to risks and uncertainties, may contain words such as "may," "will," "expect," "anticipate," "intend," "plan," "believe," "estimate" or other words indicating future results. Such statements may include, but are not limited to, statements concerning the following:

- the initiation, cost, enrollment, timing, progress and results of our research and development activities, preclinical studies and future clinical trials;
- our ability to obtain and maintain regulatory approval of our current and future product candidates, and any related restrictions, limitations, and/or warnings in the label of an approved product candidate;
- our ability to obtain funding for our operations;
- our plans to research, develop and commercialize our future product candidates;
- our strategic alliance partners' election to pursue development and commercialization;
- our ability to attract collaborators with development, regulatory and commercialization expertise;
- our ability to obtain and maintain intellectual property protection for our future product candidates;
- the size and growth potential of the markets for our current and future product candidates, and our ability to serve those markets;
- our ability to successfully commercialize our current and future product candidates;
- the rate and degree of market acceptance of our current and future product candidates;
- our ability to develop sales and marketing capabilities, whether alone or with potential future collaborators;
- regulatory developments in the United States and foreign countries;
- the performance of our third-party suppliers and manufacturers;
- the success of competing therapies that are or become available;
- the loss of key scientific or management personnel;
- our use of the proceeds from our public offerings; and
- the accuracy of our estimates regarding expenses, future revenues, capital requirements and need for additional financing.

Market, Industry and Other Data

This Annual Report contains estimates, projections and other information concerning our industry, our business and relevant markets, including data regarding the estimated size of relevant antiviral markets, patient populations, projected diagnosis rates and the perceptions and preferences of patients and physicians regarding certain therapies, as well as data regarding market research and estimates. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances that are assumed in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources that we believe to be reliable. In some cases, we do not expressly refer to the sources from which this data is derived. In that regard, when we refer to one or more sources of this type of data in any paragraph, you should assume that other data of this type appearing in the same paragraph are derived from the same sources,

unless otherwise expressly stated or the context otherwise requires.

ITEM 1. BUSINESS

Chimerix Overview

Chimerix, Inc. is a biopharmaceutical company committed to discovering, developing and commercializing medicines that improve outcomes for immunocompromised patients. We were founded in 2000 based on the promise of our proprietary lipid conjugate technology to unlock the potential of some of the most broad-spectrum antivirals by enhancing their antiviral activity and safety profiles in convenient dosing regimens. Our lead compound, brincidofovir (BCV), is in development as an oral and intravenous (IV) formulation for the prevention and treatment of DNA viruses, including smallpox, adenovirus (AdV), and the human herpesviruses.

Brincidofovir

Brincidofovir is an investigational nucleoside analog that has shown broad-spectrum antiviral activity in vitro against all five families of dsDNA (double-stranded deoxyribonucleic acid) viruses that cause human disease. In over 1,200 patients treated with BCV under a Chimerix protocol to-date, brincidofovir has been associated with a low risk of kidney or bone marrow toxicity. Oral and IV formulations of brincidofovir are currently in development, both of which deliver the active antiviral directly to the site of viral replication.

Potential indications for brincidofovir include prevention of serious viral infections in hematopoietic or stem cell transplant recipients (HCT), such as HHV-6, and treatment of serious AdV infection and disease, treatment of smallpox, and treatment of BK virus (BKV) infection in kidney and stem cell transplant recipients.

Composition of matter coverage for brincidofovir in the U.S. is currently expected to extend to October 2034.

The Company has received three orphan designations from the European Commission in relation to brincidofovir, treatment of AdV infection in immunocompromised patients, prevention of cytomegalovirus (CMV) disease, and treatment of smallpox. Companies that obtain an orphan designation are eligible for a number of incentives in the European Union (EU), including free of charge scientific advice for each orphan designation received. Compounds still meeting the criteria for orphan designation at the time of marketing approval may receive market exclusivity for 10 years from marketing approval, plus an additional two years of market exclusivity for medicines that have complied with the agreed pediatric investigational plan. The Company has also received orphan drug designation from the U.S. Food and Drug Administration (FDA) for brincidofovir treatment of smallpox.

I. Oral Formulations of Brincidofovir

Brincidofovir remains in development as an orally-administered lipid conjugate nucleotide for the treatment of serious AdV infections and as a medical countermeasure for the treatment of smallpox.

A. Oral Brincidofovir for Treatment of AdV

AdV causes gastrointestinal (GI) and upper respiratory infections, including the common cold, in individuals with a functional immune system. However, in people with a weakened immune system, AdV can lead to life-threatening infections, including pneumonia and hepatitis. Pediatric and adult patients who have undergone allogeneic HCT are at especially high risk for serious or fatal AdV infections due to profound immunodeficiency. Mortality rates of 50 to 80 percent have been reported in the literature for disseminated AdV disease. AdV infections are more common in pediatric transplant recipients than in adults; many transplant centers now actively screen their pediatric patients for AdV infection. There is currently no approved therapy for AdV infection, and although progression to disseminated disease occurs in a small proportion of patients, expected mortality for serious AdV disease is greater than 50 percent in the first three months after diagnosis.

Brincidofovir is a broad-spectrum antiviral that has demonstrated high in vitro potency against all AdV subtypes. Intracellular cleavage of brincidofovir allows cidofovir to be delivered directly to the site of viral replication. Moreover, there is a lower risk of nephrotoxicity and myelotoxicity associated with brincidofovir as compared to off-label use of intravenous cidofovir.

i. AdAPT

We initiated the AdAPT study (Adenovirus after Allogeneic Pediatric Transplantation) in December 2017. This study is targeting enrollment of 141 pediatric allogeneic HCT recipients with confirmed AdV infection. Patients are

randomized 2:1 to receive short-course oral BCV or local standard-of-care (SOC) treatment at approximately 40 sites in Europe and the United States.

The primary endpoint of the study is a comparison of the average AdV viral burden (as measured by AdV DNA levels in blood) over 16 weeks in subjects treated with short-course oral BCV versus those who receive local SOC. The study is 90% powered to show the superiority of reduced adenoviral burden in brincidofovir-treated patients compared to SOC. The study is also designed to evaluate the correlation of adenoviral burden (and its clearance) with clinical outcomes, including survival. We have faced regulatory and site initiation delays in the implementation of this study. In addition, we have observed lower than anticipated incidence at the centers that have been initiated to date. Based on a thorough re-evaluation of current screening and enrollment rates, we now project that enrollment in AdAPT will be substantially delayed beyond 2019. While some recently initiated sites are historically more active in transplantation, we continue to evaluate strategies to accelerate the time to completion of the study, including opening further AdAPT sites, and possibly re-considering the targeted number of patients for full enrollment. The Company plans to provide an update on AdAPT enrollment in mid-2019.

If successful, AdAPT may form the basis of an application for conditional or full marketing approval of brincidofovir in the EU for the treatment of AdV infection in HCT recipients. A successful trial may also further support potential continued development of oral brincidofovir in the U.S.

AdVance is the largest multicenter observational study conducted to date for AdV infection after allogeneic HCT, with established outcomes associated with the current SOC for treatment of AdV in France, Germany, Italy, Netherlands, Spain, the Czech Republic and the United Kingdom. We believe these data will help support the virologic endpoint from our ongoing AdAPT clinical trial. In February 2019, we submitted a Type C meeting request with the FDA to review the AdVance data and virologic endpoints.

B. Oral Brincidofovir for Treatment of Smallpox

We are collaborating with the Biomedical Advanced Research and Development Authority (BARDA) for the development of BCV as a potential medical countermeasure for smallpox. Efficacy is to be demonstrated via two animal models under the FDA's Animal Efficacy Rule. This rule allows for testing of investigational drugs in animal models to support the effectiveness of the drug in diseases in which human clinical studies are not ethical or feasible. In January 2019, we received positive preliminary top-line results of the in-life part of our adjunct pivotal rabbitpox efficacy study that was conducted under the Animal Efficacy Rule. The study was designed to determine the effect of administering BCV to animals at certain times (3, 4, 5 or 6 days) after inoculation with the rabbitpox virus. These preliminary results are subject to further audit, however, based on these preliminary findings the study met its primary endpoint. The topline survival results are as follows:

	BCV treatment 3 days post-infection	BCV treatment 4 days post-infection	BCV treatment 5 days post-infection	BCV treatment 6 days post-infection	No treatment (placebo)
Overall Survival	29/29 (100%)	26/29 (90%)	20/29 (69%)	20/29 (69%)	8/28 (29%)
P-value vs. Group 5	<0.0001	<0.0001	0.0014	0.0014	0

The differences in survival rate observed between each group of animals that received BCV and the animals that did not are statistically significant. Data from this study are in-line with those reported in 2015 from our first pivotal study in the rabbitpox model.

In February 2019, we initiated a pivotal study in the mouse ectromelia model, which constitutes our second animal model as described in the Animal Efficacy Rule. We anticipate data from this study in the second half of 2019 and, contingent upon the results of the animal efficacy studies, we plan to submit marketing applications in 2020.

C. Oral Brincidofovir Expanded Access Program

We continue to fulfill requests for orally administered brincidofovir via our expanded access programs. In 2018, we granted almost 340 requests for brincidofovir for the treatment of AdV, highlighting the continued unmet need in this area.

II. IV Formulation of Brincidofovir

Our ability to provide brincidofovir in oral and IV formulations enables development across multiple indications and populations with the potential for best-in-class efficacy and safety. In animal studies and multiple dose administration in healthy subjects, IV BCV has shown the potential for less GI injury compared to oral brincidofovir, even with

higher plasma drug concentrations and longer-term dosing.

A. IV Brincidofovir Multiple Ascending Dose Study in Healthy Subjects

In late 2017, we completed the multiple ascending dose (MAD) study of IV BCV in healthy subjects. This Phase 1 study evaluated the safety, tolerability and pharmacokinetics (PK) of IV BCV 10 mg given twice weekly and IV BCV 20 mg given once weekly in healthy subjects for two to four weeks. IV BCV was well-tolerated at all dose levels, with no dose-limiting clinical adverse events. Importantly, there was no diarrhea reported for IV BCV 10 mg dosed twice weekly, a dose that provides drug levels equivalent to oral BCV 100 mg which demonstrated antiviral activity in previous late-stage clinical studies. Non-clinically-relevant elevations in serum transaminases were noted as seen in previous studies of oral BCV.

B. Ongoing Phase 2 Studies (210/211)

Following completion of the MAD study of IV brincidofovir in healthy subjects, we have started two Phase 2 open label dose-ranging studies of IV BCV in patients with active AdV.

Studies of IV BCV in AdV virally-infected patients are ongoing. These studies may provide data on other viral infections such as CMV and/or BKV in patients with multi-viral infections. These studies are the first-in-patient studies to demonstrate the safety and tolerability and pharmacokinetic profile of multiple doses of IV BCV in adult HCT recipients. We will also evaluate the relationship between dose and change from baseline in AdV in blood and stool. Similar to AdAPT, we have faced regulatory and site initiation delays in the implementation of these studies. We have also observed lower than anticipated incidence at the study 210/211 centers that have been initiated, which has caused enrollment to occur more slowly than expected. We plan to provide a study update in mid-2019.

Data from these studies will inform the dose and dosing regimen for our potential Multi Viral Protection (MVP)-Peds study and potential studies of IV BCV for other DNA viruses, such as BKV or HHV-6.

The improved drug concentrations in the central nervous system (CNS) achieved with IV brincidofovir in animals could support the study of IV brincidofovir in viral CNS infections such as herpes encephalitis, HHV-6 encephalitis, JC virus infection.

CMX521 for Norovirus

CMX521 is a nucleoside analog identified from our proprietary Chemical Library which targets the norovirus polymerase, a part of the virus that is common to all strains and is required for viral replication. It therefore has the potential to be active against the multiple genetically diverse norovirus strains that circulate each year and cause disease in humans.

We previously presented the safety and tolerability data from a Phase 1 study of CMX521, which supported continued development of the first small molecule in clinical development for prophylaxis or treatment of norovirus. Evaluation of active antiviral concentrations in GI biopsies indicate that improved intracellular delivery is needed prior to conducting efficacy studies. The norovirus research and development program has been paused indefinitely.

CMX157

CMX157, our second clinical stage nucleoside analog, uses the same proprietary lipid technology as brincidofovir to deliver high intracellular concentrations of the potent antiviral drug, tenofovir. Tenofovir, marketed under the brand name Viread® and in multiple fixed-dose combinations, is widely used for the treatment of HIV and hepatitis B virus (HBV) infection. In December 2014, we entered into a licensing agreement with ContraVir Pharmaceuticals (Nasdaq: CTRV) for the development and commercialization of CMX157 for certain antiviral indications. Under the terms of the agreement, ContraVir has sole responsibility with respect to the control of the development and commercialization of CMX157.

Lipid Conjugate Technology and Our Chemical Library

Lipid Conjugate Technology

Our proprietary lipid conjugate technology is used to covalently modify a drug molecule with a lipid side-chain that mimics a naturally occurring phospholipid component of cellular membranes. The lipid mimic can then utilize natural uptake pathways to achieve oral bioavailability, enhance uptake into cells, and potentially to avoid many toxicities.

We believe that our lipid conjugate technology can be used to develop new drugs from parent molecules having a known mechanism of action but potentially with an improved safety, efficacy, and/or ADME (absorption/distribution/metabolism/excretion) profile relative to the parent. Preclinical studies and in vitro assessments of a number of drugs, including some that are approved, have shown specific improvements in biological activity compared with the parent drug.

The most advanced example of our proprietary lipid conjugate technology is brincidofovir, which was developed to improve the efficacy and safety of an approved drug, cidofovir. Use of cidofovir has been limited by significant toxicities, particularly kidney toxicity. Unlike cidofovir, the lipid-conjugated brincidofovir molecule is not actively concentrated in the kidneys, but does effectively deliver the active antiviral to cells. Brincidofovir may have a higher benefit-risk ratio that allows expanded use relative to cidofovir, for example in prevention of AdV disease, and potentially protection from or treatment of other DNA viruses.

Chimerix Chemical Library

The Chimerix Chemical Library contains over 10,000 heterocyclic ring systems and nucleosides, the majority of which were originally synthesized in the laboratory of Dr. Leroy Townsend at the University of Michigan. This library includes approximately 3,500 nucleoside analog compounds, most of which are candidates for lipid conjugation. We have an active discovery program focusing on viral diseases in which there is significant unmet medical need. We periodically screen the library for activity against viral targets for which limited or no therapies are currently available.

Evaluation of External Opportunities to Strengthen our Pipeline

We are looking at business development opportunities as a means to complement our existing pipeline with technologies that will take advantage of our strengths. We are actively seeking opportunities to grow our business through the acquisition of, or investment in, other companies, through strategic relationships, or through in-licensing of complementary compounds and products.

Significant Agreements

ContraVir Pharmaceuticals

In December 2014, we entered into a license agreement with ContraVir Pharmaceuticals (Nasdaq: CTRV) for the development and commercialization of CMX157 for certain antiviral indications. Under the terms of the agreement, ContraVir has sole responsibility with respect to the control of the development and commercialization of CMX157.

In exchange for the license to CMX157 rights, we received an upfront payment consisting of 120,000 shares of ContraVir Series B Convertible Preferred Stock with a stated value of $1.2 million. In addition, we are eligible to receive up to approximately $20 million in clinical, regulatory and initial commercial milestones in the United States and Europe, as well as royalties and additional milestones based on commercial sales in those territories. Either party may terminate the license agreement upon the occurrence of a material breach by the other party (subject to standard cure periods), or upon certain events involving the bankruptcy or insolvency of the other party. ContraVir may also terminate the license agreement without cause on a country-by-country basis upon sixty days' prior written notice.

In September 2016, we converted our shares of ContraVir Series B Convertible Preferred Stock into shares of ContraVir common stock.

BARDA

In February 2011, we entered into a contract with BARDA for the advanced development of brincidofovir as a medical countermeasure in the event of a smallpox release. BARDA is a division of the U.S. Department of Health and Human Services (DHHS) in the Office of the Assistant Secretary for Preparedness and Response that supports the advanced research and development, manufacturing, acquisition and stockpiling of medical countermeasures. The scope of work for the contract includes preclinical, clinical and manufacturing development activities that fall into the following areas: non-clinical animal efficacy studies; clinical activities; manufacturing activities; and all associated regulatory, quality assurance, management, and administrative activities.

Under the contract, BARDA will reimburse our costs, plus pay us a fixed fee, for the research and development of brincidofovir as a treatment of smallpox infections. The contract consists of an initial performance period, referred to as the base performance segment which ended on May 31, 2013, plus up to four extension periods, referred to as option segments, each of which may be exercised at BARDA's sole discretion. We must complete agreed upon milestones and deliverables in each discrete work segment before the next option segment is eligible to be exercised.

Under the contract as currently in effect, if each follow-on option segment is exercised by BARDA, we may receive up to $75.8 million in expense reimbursement and $5.3 million in fees.

We substantially completed the first option segment of the contract on August 28, 2014. In September 2014, we were awarded a contract extension for a second option segment providing an additional $17.0 million. In August 2016, the contract was amended to provide an additional $535,000, in December 2017 the contract was amended to increase funding by an additional $4.1 million, and in January 2019 the contract was amended to increase funding by an additional $2.3 million for the performance of the second option segment, which is scheduled to end on August 1, 2019. On September 11, 2015, BARDA exercised option segment three, which provided approximately $12.9 million in funding for the performance of the segment. In December 2017, BARDA decreased the scope of this segment by removing a potential second pivotal ectromelia virus study which decreased the funding of this option segment by $1.3 million to a total award of $11.6 million; option segment three is scheduled to end on March 30, 2019. Of the $75.8 million expense reimbursement and $5.3 million in fees that we may receive, approximately $74.3 million in expense

reimbursement and fees has been funded. As of December 31, 2018, of the total funding we had invoiced an aggregate of $62.6 million with respect to the base performance segment and the first three extension periods.

Pursuant to the contract, Chimerix and the U.S. government share the rights to any inventions made in the performance of our work under the contract. Specifically, the U.S. government retains a nonexclusive, nontransferable, irrevocable, paid up license to any invention made in the performance of our work under the contract, provided, however, that the U.S. government may, under certain circumstances, including circumstances involving public health and safety, license such inventions to third parties without our consent. There have been no inventions made to date under the BARDA contract.

The contract may be terminated by BARDA ten days after giving us notice of a material default which remains uncured for ten days. In addition, BARDA is also permitted under applicable law to terminate the contract if it is in the U.S. government's best interest.

In April 2015, the DHHS, Office of the Assistant Secretary for Preparedness and Response, BARDA posted a notice of intent to use other than full and open competition (Notice of Intent) to award a sole source contract to us for the procurement of brincidofovir for the treatment of smallpox.

In July 2015, BARDA issued a RFP entitled "2015 Procurement of a Second Smallpox Antiviral Drug for the Strategic National Stockpile." In August 2015, we submitted a response to the RFP and we subsequently engaged in discussions with BARDA regarding our response. The issuance of that RFP did not culminate with agreement for the sole source supply of brincidofovir for the Strategic National Stockpile.

There are no RFPs for procurement of a smallpox antiviral pertaining to brincidofovir that are currently pending.

In the event a new RFP is issued we will likely submit a proposal. In the event that our proposal is chosen (potentially among several competing proposals) and before we can enter into a contract we must negotiate its terms, including the price and delivery schedule. In addition, as a governmental agency, BARDA's ability to enter into a contract is subject to continued funding for this purpose, which can change at any time. We remain in discussions with BARDA regarding the potential to supply brincidofovir to the Strategic National Stockpile, however, there can be no assurances regarding any such procurement. The Company continues to receive funding under an advanced research and development contract for the development of brincidofovir for the treatment of smallpox. We are currently evaluating brincidofovir for efficacy in two different animal models to support potential approval under the FDA's Animal Efficacy Rule.

The Regents of the University of California

In May 2002, we entered into a license agreement with The Regents of the University of California (UC) under which we obtained an exclusive, worldwide license to UC's patent rights in certain inventions (the UC Patent Rights) related to lipid-conjugated antiviral compounds and their use, including certain patents relating to brincidofovir and CMX157. Under the license agreement, we are permitted to research, develop, manufacture and commercialize products utilizing the UC Patent Rights for all human and veterinary uses, and to sublicense such rights subject to certain sublicensing fees and royalty payments.

In consideration for the rights granted to us under the license agreement, we issued UC an aggregate of 64,788 shares of our common stock. In connection to the development and commercialization of brincidofovir and CMX157, we could be required to pay UC up to an aggregate of $3.4 million in milestone payments, assuming the achievement of all applicable milestone events under the license agreement. In addition, upon commercialization of any product utilizing the UC Patent Rights, which would include brincidofovir or CMX157, we will be required to pay low single

digit royalties on net sales of such product.

The license agreement requires that we diligently develop, manufacture and commercialize compounds that are covered by the UC Patent Rights, and we have agreed to meet certain development and commercialization milestones. UC may, at its option, either terminate the license agreement or change the license granted from an exclusive license to a non-exclusive license if we fail to meet such development and commercialization milestones. We are currently in compliance with these milestone requirements.

University of Michigan

In 2006, we entered into a license agreement with The Regents of the University of Michigan (UM) under which we obtained an exclusive, worldwide license to UM's patent rights in certain inventions (UM Patent Rights) related to certain compounds originally synthesized in the laboratory of Dr. Leroy Townsend at the University of Michigan. Under the license agreement, we are permitted to research, develop, manufacture and commercialize products utilizing the UM Patent Rights, and to sublicense such rights subject to certain sublicensing fees and royalty payments.

In consideration for the rights granted to us under the license agreement, we have paid UM an aggregate of $70,000 in fees and in January 2017 issued UM an aggregate of 33,058 shares of our common stock. In connection with our commercialization or sublicensing of certain products covered by the license agreement, including CMX521, we could be required to pay royalties on net sales of such products ranging from 0.25% to 2%. Beginning in 2024, we are also subject to certain minimum annual royalty payments.

The UM license agreement requires that we use commercially reasonable efforts to develop and make commercially available licensed products as soon as practicable. Specifically, we have agreed to make the first commercial sale of a licensed product by June of 2026. UM may terminate the license agreement if we materially breach the license agreement. We are currently in compliance with our milestone requirements.

Commercial Operations

We anticipate that our first commercial indication for brincidofovir may be in the treatment of AdV infections in pediatric allogeneic HCT recipients. In anticipation of potential regulatory approval and commercial launch of brincidofovir, we are building select commercial functions tied to key milestones. These milestones include the availability of data from our IV brincidofovir studies, and other potential trials or studies, potential submission of marketing applications for brincidofovir, and anticipated approval (or PDUFA) dates.

Patients who undergo an allogeneic HCT are likely to be treated at a small number of major medical centers by specialized teams of physicians and healthcare providers. There are approximately 200 HCT transplant centers in the U.S. and 300 in the EU-5. The management of therapies for transplant patients is largely the responsibility of transplant physicians, infectious disease specialists, and clinical pharmacists who oversee post-transplant therapies. These clinicians focus on prevention and management of post-transplant infections as one of their key priorities. Practice patterns for the management of transplant patients and post-transplant viral infections vary from institution to institution and are highly driven by research activities, data and publications.

If brincidofovir is approved for the treatment of AdV infection, we believe it is possible for us to commercialize brincidofovir in the United States. We anticipate that this would entail a relatively small commercial infrastructure, which may include a contract sales force, partner sales force, or internal team. While our commercialization efforts may initially be focused on health care providers who are responsible for treating AdV, this commercial infrastructure would serve as the foundation for an expanded commercial presence based on lifecycle indications and other opportunities within the corporate portfolio.

Outside of the United States, subject to obtaining necessary marketing approvals, we may seek to commercialize brincidofovir ourselves or through distribution or other collaboration arrangements. If we elect to develop brincidofovir for other DNA viral indications, we would plan to do so selectively either on our own or by establishing alliances with one or more pharmaceutical company collaborators, depending on, among other things, the applicable indications, the related development costs, reimbursement complexities and our available resources.

Competition

Our industry is highly competitive and subject to rapid and significant technological change. While we believe that our therapeutic experience, scientific and commercial knowledge provide us with competitive advantages, we will face competition from large and small pharmaceutical, biotechnology companies, including specialty pharmaceutical and generic drug companies, and other emerging technologies.

We believe that the key competitive factors that will affect the commercial success of brincidofovir and our other product candidates are the efficacy, safety and tolerability profile and the risk:benefit trade-off compared to alternative therapies or procedures. Securing market access and reimbursement will be an important element of product uptake and market penetration. Our commercial opportunity could be negatively impacted if our competitors develop or market products or other technologies that are more effective, better tolerated, safer, more convenient or have greater market access than brincidofovir, or obtain regulatory approval for their products more rapidly than we do. In addition, our ability to compete will be affected by the availability of generic products.

If approved, brincidofovir would compete with a number of existing products and other product candidates that target serious viral infections, including drugs and vaccines which demonstrate efficacy against viruses that affect our target patient populations. We believe brincidofovir has potential benefits over the competitive products, including the potential to be the first antiviral indicated for treatment of disseminated AdV in allogeneic HCT recipients. Based on market research, competing products that are currently used, or being developed for use, to treat AdV include and are not limited to:

- cidofovir, a drug that is sold by generic manufacturers; and
- patient-specific T-cell therapies.

Other product candidates currently in development may compete against brincidofovir for the prevention or mitigation of CMV infection in a variety of settings, including:

- letermovir (marketed under the trade name PREVYMIS), an anti-CMV drug recently approved for the prevention of CMV infections in adult HCT recipients pursuant to an exclusive worldwide license agreement between AiCuris GmbH & Co. KG and Merck & Co., Inc.;
- maribavir, an antiviral owned by Shire plc, currently in Phase 3 trials for the treatment of CMV resistant or refractory CMV infections in both HCT and SOT adult patients, and for preemptive use in adult HCT patients; and
- patient-specific T-cell therapies directed at antigens of CMV and other dsDNA viruses.

Furthermore, we anticipate that we will face intense and increasing competition as new products enter the market, as advanced technologies become available and as increasing numbers of generic formulations of currently branded products become available.

Changes in the health care system may limit our ability to price brincidofovir or our other product candidates at a level that would allow recovery of our research and development costs and may impede our ability to generate or maintain a profit.

We believe that brincidofovir has potential benefits over existing and potential competitive products as described in more detail under “Business - Brincidofovir.” As a result, we believe that brincidofovir should be well positioned to gain market share if we obtain the required regulatory approval. However, even with those benefits, we may not be able to make promotional claims that brincidofovir is superior to these competing products without conducting additional studies, which delivers differentiated data, and brincidofovir may be unable to compete successfully against these products. See “Risk Factors - Risks Related to Commercialization of Our Product Candidates.”

Our Intellectual Property

We strive to protect and enhance the proprietary technologies we believe are important to our business, including by seeking and maintaining patents intended to cover our products and compositions, their methods of use and any other inventions that are important to the development of our business. We also rely on trade secrets to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

Our success will depend significantly on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business, defend and enforce our patents, maintain licenses to our intellectual property owned by third parties, preserve the confidentiality of our trade secrets and operate without infringing the valid and enforceable patents and proprietary rights of third parties.

We believe that we have a strong intellectual property position and substantial know-how relating to the development and commercialization of our lipid conjugate technology platform and the Chimerix Chemical Library.

At February 15, 2019, our worldwide patent portfolio included:

- 123 patents or patent applications that we own or have in-licensed from academic institutions, related to brincidofovir and CMX157, which represented a slight decrease over the number of patents in our patent portfolio at the end of fiscal 2017;
- This includes 87 US and foreign exclusively and jointly owned patents and 36 US and foreign applications related to brincidofovir and CMX157. Granted European patents are counted as one patent and have been validated throughout Europe;
- 19 jointly-owned patents or patent applications related to our agreement with the UM regarding our proprietary Chemical Library; and
- One international patent application owned exclusively by Chimerix directed to a morphic form of a compound from the Chemical Library.

In 2015, U.S. Patent No. 8,962,829 covering a method of synthesis and the commercial morphic form of brincidofovir was issued to Chimerix. With the addition of this patent, composition of matter coverage for brincidofovir in the U.S. is expected to extend to October 2034.

Patents generally have a term of twenty years from the date they are filed. As our patent portfolio has been built over time, the remaining terms of the individual patents across our patent portfolio vary. We believe that our patents and patent applications are important for maintaining the competitive differentiation of our lipid-antiviral-conjugate technology platform and the Chimerix Chemical Library, enhancing our freedom of action to sell our antivirals, upon appropriate regulatory approvals, in markets in which we choose to participate, and maximizing our return on research and development investments. No single patent is in itself essential to the conduct of our business as a whole.

We are also open to expanding our intellectual property portfolio through licensing intellectual property from third parties as we deem appropriate. We have granted and will continue to grant to others licenses under our patents when we consider these arrangements to be in our interest.

Manufacturing

We do not own or operate and we do not expect to own or operate facilities for product manufacturing, storage and distribution, or testing. In the past, we have relied on third-party manufacturers for supply of our lead product candidate, brincidofovir, as well as our other product candidates. We expect that in the future we will rely on such manufacturers for supply of drug substance and drug product that will be used in clinical trials of brincidofovir, as well as for commercial purposes should brincidofovir be approved. When produced on a commercial scale, we expect that cost-of-goods-sold relating to brincidofovir will generally be in-line with that of other small-molecule pharmaceutical compounds.

The manufacturing process for brincidofovir drug substance is relatively straight-forward and generally in-line with other small molecule pharmaceutical compounds in terms of cost and complexity. The process is robust and reproducible, does not require dedicated reactors or specialized equipment, uses common synthetic chemistry and readily available materials, including off-the-shelf and made-to-order starting materials, and is readily transferable.

Our current drug substance supply chain for brincidofovir involves various contractors that supply the raw materials for the drug substance process, a contract manufacturer for an intermediate, and a contract manufacturer for the drug substance. We have completed transferring our current commercial drug substance manufacturing process to our selected contractor that will produce the commercial supply of drug substance and began process validation during 2015. Manufacturers of drug components must meet certain FDA qualifications with respect to manufacturing standards. At present, we have qualified only one firm as a supplier of drug substance. We continually assess our manufacturing needs and may seek to engage additional qualified vendors as circumstances dictate. Changes in our requirements may require revalidation of the manufacturing process at a different scale and potentially at a different contractor depending on the necessary scale, infrastructure and technical capabilities. To ensure continuity in our supply chain, we plan to establish supply arrangements with alternative suppliers for certain portions of our supply chain, as appropriate.

Our drug products (tablets, oral suspension, intravenous solution or lyophilized powder for solution) are also manufactured under contract. We have completed development and transfer of our current commercial suspension and tablet manufacturing process to our selected contractor that will produce commercial supplies. We initiated validation of these processes in 2018. The intravenous formulation of brincidofovir is in early-stage development.

Manufacturing is subject to extensive regulations that impose various procedural and documentation requirements, which govern record keeping, manufacturing processes and controls, personnel, quality control and quality assurance, among others. Our systems and contractors are required to be in compliance with these regulations, and this is assessed regularly through monitoring of performance and a formal audit program. We have personnel with extensive technical, manufacturing, analytical and quality experience and strong project management discipline to oversee contract manufacturing and testing activities, and to compile manufacturing and quality information for our regulatory submissions.

Pursuant to our license agreement with ContraVir, the manufacture of CMX157 is under the control and direction of ContraVir.

Government Regulation and Product Approval

Government authorities in the United States, at the federal, state and local level, and government authorities of member states of the EU and other countries extensively regulate, among other things, the research, development, testing, manufacture, quality

control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of products such as those we are developing. Any product candidate that we develop must be approved by the FDA or EMA before it may be legally marketed in the United States or EU and in other countries by the responsible national regulatory agency before it may be legally marketed.

U.S. Drug Development Process

In the United States, the FDA regulates drugs under the Federal Food, Drug and Cosmetic Act (FDCA), and implementing regulations. Drugs are also subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, FDA approval process or after FDA approval, may subject an applicant to administrative or judicial civil or criminal sanctions. FDA sanctions could include refusal to approve pending applications, withdrawal of an approval, clinical hold, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, debarment, restitution, disgorgement or civil or criminal penalties. Any agency or judicial enforcement action, whether before or after the FDA approval process, could have a material adverse effect on us. The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of nonclinical laboratory tests, animal studies and formulation studies according to good laboratory practices (GLP), or other applicable regulations;
- submission to the FDA of an application for an IND, which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials according to the FDA's regulations commonly referred to as current good clinical practices (GCPs), to establish the safety and efficacy of the proposed drug for its intended use;
- submission to the FDA of a NDA for a new drug;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the drug is produced to assess compliance with the FDA's current good manufacturing practice standards (cGMP), to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- potential FDA inspection of the nonclinical and clinical trial sites that generated the data in support of the NDA; and
- FDA review of the NDA.

The lengthy process of seeking required approvals and the continuing need for compliance with applicable statutes and regulations require the expenditure of substantial resources and approvals are inherently uncertain.

Before testing any compounds with potential therapeutic value in humans, the drug candidate enters the preclinical testing stage. Preclinical tests, also referred to as nonclinical studies, include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies to assess the potential safety and activity of the drug candidate. The conduct of the preclinical tests must comply with federal regulations and requirements including GLP. The sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol to the FDA as part of the IND. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA places the clinical trial on a clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA may also impose clinical holds on a drug candidate at any time before or during clinical trials due to safety concerns or non-compliance. Accordingly, we cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that suspend or terminate such trial.

Clinical trials involve the administration of the drug candidate to healthy subjects or affected patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety. Each protocol must be submitted to the FDA as part of the IND. Patients not meeting protocol inclusion and exclusion criteria may be considered for our expanded access program under the IND. Clinical trials must be conducted in accordance with the FDA's regulations comprising the good clinical practices requirements. Further, each clinical trial must be reviewed and approved by an independent institutional review board (IRB), at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the form and content of the informed consent that must be signed by each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed.

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

- Phase 1. The drug is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.
- Phase 2. The drug is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance, optimal dosage and dosing schedule.
- Phase 3. Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed 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. Generally, two adequate and well-controlled Phase 3 clinical trials are required by the FDA for approval of an NDA.

Post-approval clinical trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These clinical trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication.

Annual progress reports detailing the results of the clinical trials must be submitted to the FDA and written IND safety reports must be promptly submitted to the FDA and the investigators for serious and unexpected adverse events or any finding from tests in laboratory animals that suggests a significant risk for human subjects. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA or the sponsor or its data safety monitoring board may suspend a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB’s requirements or if the drug has been associated with unexpected serious harm to patients.

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

U.S. Review and Approval Processes

The results of product development, nonclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. The submission of an NDA is subject to the payment of substantial user fees; a waiver of such fees may be obtained under certain limited circumstances.

In addition, under the Pediatric Research Equity Act (PREA), an NDA or supplement to an NDA must contain data to assess the safety and effectiveness 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. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any drug for an indication for which orphan designation has been granted.

The FDA reviews all NDAs submitted to determine if they are substantially complete before it accepts them for filing; this initial review period prior to accepting the NDA for filing is 2 months in duration. 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 the Prescription Drug User Fee Act (PDUFA), the FDA has 10 months from the date of accepting the NDA for filing in which to complete its initial review of a standard NDA and respond to the applicant, and six months for a priority NDA. The FDA does not always meet its PDUFA goal dates for standard and priority NDAs. The review process and the PDUFA goal date may be extended if the FDA requests or the NDA sponsor otherwise provides additional information or clarification regarding information already provided in the submission without prior agreement reached at a pre-submission meeting.

After the NDA submission is accepted for filing, the FDA reviews the NDA to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with cGMP to assure and preserve the product's identity, strength, quality and purity. The FDA may refer applications for novel drug or biological products or drug or biological products which present difficult questions of safety or efficacy to an advisory committee, typically

a panel that includes clinicians and other experts, for review, evaluation and 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. During the drug approval process, the FDA also will determine whether a risk evaluation and mitigation strategy (REMS), is necessary to assure the safe use of the drug. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS. The FDA will not approve the NDA without a REMS, if required.

Before approving an NDA, the FDA will inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure that the clinical trials were conducted in compliance with IND study requirements. If major issues with trial conduct are identified at a site, data collected from that site can be determined to be unacceptable for supporting the application. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable it will outline the deficiencies in the submission and often will request additional testing or information.

The NDA review and approval process is lengthy and difficult and the FDA may refuse to approve an NDA if the applicable regulatory criteria are not satisfied or may require additional clinical data or other data and information. Even if such data and information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data. The FDA will issue a complete response letter if the agency decides not to approve the NDA. The complete response letter usually describes all of the specific deficiencies in the NDA identified by the FDA. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical trials. Additionally, the complete response letter may include recommended actions that the applicant might take to place the application in a condition for approval. If a complete response letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. In addition, the FDA may require post marketing clinical trials, sometimes referred to as Phase 4 clinical trials testing, which involves clinical trials designed to further assess a drug’s safety and effectiveness and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biological product intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making a drug or biological product available in the United States for this type of disease or condition will be recovered from sales of the product. Orphan product designation must be requested before submitting an NDA. After the FDA grants orphan product designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug or biological product for the same indication for seven

years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity. Competitors, however, 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. Orphan product exclusivity also could block the approval of a product for seven years if a competitor obtains approval of the same drug or biological product as defined by the FDA or if a drug candidate is determined to be contained within the competitor's product for the same indication or disease. If a drug or biological product designated as an orphan product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan product exclusivity.

Expedited Development and Review Programs

The FDA has a number of programs that are intended to expedite or facilitate the process for reviewing new drugs and biological products for serious conditions that meet certain criteria. Specifically, new drugs and biological products are eligible for Fast Track, Breakthrough Therapy, and/or Priority Review designation if they are intended to treat a serious or life-threatening condition

and demonstrate the potential to address unmet medical needs for the condition. Fast Track designation applies to the combination of the product and the specific indication for which it is being studied. Breakthrough Therapy designation is for a drug that is intended to treat a serious condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement on a clinically significant endpoint(s) over available therapies. Unique to Fast Track and Breakthrough Therapy products, the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA.

Any product submitted to the FDA for marketing approval, including Fast Track and Breakthrough Therapy programs, may also be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. Any product is eligible for priority review if it has the potential to provide safe and effective therapy where no satisfactory alternative therapy exists or a significant improvement in the treatment, diagnosis or prevention of a disease compared to marketed products. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug or biological product designated for priority review in an effort to facilitate the review. Additionally, a product may be eligible for accelerated approval. Drug or biological products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval, which means that they may be approved on the basis of adequate and well-controlled clinical trials establishing that the product has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity. As a condition of approval, the FDA may require that a sponsor of a drug or biological product receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials to establish safety and efficacy for the approved indication. In addition, the FDA currently requires as a condition for accelerated approval pre-review of promotional materials, which could adversely impact the timing of the commercial launch of the product. Fast Track, Breakthrough, and Priority Review designations and accelerated approval do not change the standards for approval but may expedite the development or approval process.

Animal Efficacy Rule

FDA permits the approval of certain drugs and biologics that are intended to reduce or prevent serious or life-threatening conditions based on evidence of safety from clinical trial(s) in healthy subjects and effectiveness from appropriate animal studies when human efficacy studies are not ethical or feasible. These regulations, which are known as the “Animal Rule”, authorize the FDA to rely on animal studies to provide evidence of a product’s effectiveness under circumstances where there is a reasonably well-understood mechanism for the activity of the agent. Under these requirements, and with the FDA’s prior agreement, drugs used to reduce or prevent the toxicity of chemical, biological, radiological or nuclear substances may be approved for use in humans based on evidence of effectiveness derived from appropriate animal studies and any additional supporting data. Products evaluated under this rule must demonstrate effectiveness through pivotal animal studies, which are generally equivalent in design and robustness to Phase 3 clinical studies. The animal study endpoint must be clearly related to the desired benefit in humans and the information obtained from animal studies must allow for selection of an effective dose in humans. Safety under this rule is established under preexisting requirements, including safety studies in both animals (toxicology) and humans. Products approved under the Animal Rule are subject to additional requirements including post-marketing study requirements, restrictions imposed on marketing or distribution or requirements to provide information to patients.

Expanded access programs

Many jurisdictions allow the supply of unauthorized medicinal products in the context of strictly regulated and exceptional early access programs, and some countries may provide reimbursement for drugs provided in the context

of such programs. The promotion, advertising and marketing of unauthorized medicinal products is generally prohibited, and authorization for early access programs must generally be obtained from regulatory authorities, which might not grant such authorization. To provide expanded access, sponsors must submit detailed regulatory information to the FDA. FDA authorization depends on several different factors, including whether expanded access will interfere with related clinical trials or drug development. In addition to the FDA's early access program, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017, or the Right to Try Act, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase I 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 pharmaceutical manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act. Sponsors may not promote products as safe or effective for expanded-access uses.

Post-Approval Requirements

Any drug products for which we or our strategic alliance partners receive FDA approvals are subject to continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse experiences with the product, providing the FDA with updated safety and efficacy information, product sampling and distribution requirements, complying with certain electronic records and signature requirements and complying with FDA promotion and advertising requirements. These promotion and advertising agreements include, among others, standards for direct-to-consumer advertising, promoting drugs for uses or in patient populations that are not described in the drug's approved labeling (known as "off-label use"), industry-sponsored scientific and educational activities, and promotional activities involving the internet. Failure to comply with FDA requirements can have negative consequences, including adverse publicity, enforcement letters from the FDA, mandated corrective advertising or communications with doctors, and civil or criminal penalties. Although physicians may prescribe legally available drugs for off-label uses, manufacturers may not market or promote such off-label uses.

We will rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of any products that we may commercialize. Our strategic alliance partners may also utilize third parties for some or all of a product we are developing with such strategic alliance partner. Manufacturers of our products are required to comply with applicable FDA manufacturing requirements contained in the FDA's cGMP regulations. cGMP regulations require among other things, quality control and quality assurance as well as the corresponding maintenance of records and documentation. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. Discovery of problems with a product after approval may result in restrictions on a product, manufacturer, or holder of an approved NDA, including withdrawal of the product from the market. In addition, changes to the manufacturing process generally require prior FDA approval before being implemented and other types of changes to the approved product, such as adding new indications and additional labeling claims, are also subject to further FDA review and approval.

The FDA also may require post-marketing testing, known as Phase 4 testing, risk minimization action plans and surveillance to monitor the effects of an approved product or place conditions on an approval that could restrict the distribution or use of the product.

U.S. Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of the FDA approval of the use of our drug candidates, some of our United States patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of an NDA and the approval of that application. Only one patent applicable to an approved drug is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The United States Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may apply for restoration of patent term for one of our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant NDA.

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

exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness. Pediatric exclusivity is another type of regulatory market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA-issued "Written Request" for such a trial.

US Health Care Laws

Our operations may be subject to federal and state health care laws and regulations including, without limitation: anti-kickback statutes, false claims statutes, patient data privacy and security laws, and physician payment transparency laws and regulations, many of which may become more applicable if our product candidates are approved and we begin commercialization. If our operations are found to be in violation of any of these laws or regulations, we may be subject to penalties, including administrative, civil and criminal penalties, damages, fines, disgorgement, imprisonment, exclusion from participation in federal healthcare programs, and additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, as well as contractual damages, reputational harm, diminished profits and future earnings, and the curtailment or restructuring of our operations.

Reimbursement

Sales of pharmaceutical products depend in significant part on the availability of third-party reimbursement. Third-party payers include government health programs such as Medicare and Medicaid, managed care providers, private health insurers and other organizations. These third-party payers are increasingly challenging the price and examining the cost-effectiveness of medical products and services, including prescription drugs. In addition, significant uncertainty exists as to the reimbursement status of newly approved prescription drugs and other healthcare products. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the cost-effectiveness of any of our products that is successfully developed and approved. Our product candidates may not be considered cost-effective. It is time consuming and expensive to seek reimbursement from third-party payers. Reimbursement may not be available or sufficient to allow the sale of any of our products that is successfully developed and approved on a competitive and profitable basis.

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA), established the Medicare Part D program to provide a voluntary prescription drug benefit to Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities to provide coverage of outpatient prescription drugs. Part D plans include both stand-alone prescription drug benefit plans and prescription drug coverage as a supplement to Medicare Advantage plans. Unlike Medicare Parts A and B, Part D coverage is not standardized. Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each Part D prescription drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, although not necessarily all of the drugs within each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee.

It is not clear what long-term effect the MMA will have on the prices paid for currently approved drugs and the pricing options for newly approved drugs. Government payment for some of the costs of prescription drugs may increase demand for any of our products that is successfully developed and approved. However, any negotiated prices for our products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain. Moreover, although the MMA applies only to drug benefits for Medicare beneficiaries, private payers often

follow Medicare coverage policy and payment limitations in setting their own payment rates. Accordingly, any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payers.

We expect that there will continue to be a number of federal and state proposals to implement governmental pricing controls and limit the growth of healthcare costs, including the cost of prescription drugs. Currently, Medicare is prohibited from negotiating directly with pharmaceutical companies for drugs. However, the U.S. Congress may in the future consider legislation that would lift the ban on federal negotiations.

The American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. A plan for the research would be developed by the U.S. Department of Health and Human Services (DHHS), Agency for Healthcare Research and Quality and the National Institutes of Health, and periodic reports on the status of the research and related expenditures would be made to the U.S. Congress. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private payers, it is not clear whether research would have any effect on the sales of any of our products that are successfully developed and approved, if the product or the

condition that it is intended to treat becomes the subject of a study. It is also possible that comparative effectiveness research demonstrating benefits of a competitor's product could adversely affect the sales of any of our products that is successfully developed and approved. If third-party payers do not consider our products to be cost-effective compared to other available therapies, they may not cover our products after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, ACA), is expected to have a significant impact on the health care industry. The ACA is expected to expand coverage for the uninsured while at the same time containing overall healthcare costs. Among other things, the ACA expands and increases industry rebates for drugs covered under Medicaid programs and make changes to the coverage requirements under the Medicare Part D program. We cannot predict the impact of the ACA on pharmaceutical companies because some of the ACA's reforms require the promulgation of detailed regulations to implement the statutory provisions, which has not yet occurred. In addition, there have been judicial and Congressional challenges to certain aspects of the ACA, as well as recent efforts by the Trump administration to repeal and replace certain aspects of the ACA, and we expect such challenges to continue. Since January 2017, President Trump has signed two Executive Orders and other directives designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the ACA have been enacted. Legislation enacted in 2017 (H.R. 1, "An Act to provide for reconciliation pursuant to titles II and V of the concurrent resolution on the budget for fiscal year 2018"), informally titled the Tax Cuts and Jobs Act of 2017, or Tax Act, includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." On January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain fees mandated by the ACA, including the so-called "Cadillac" tax on certain high-cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. The Bipartisan Budget Act of 2018, or the BBA, among other things, amended the ACA, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, and also increases in 2019 the percentage that a drug manufacturer must discount the cost of prescription drugs from 50 percent to 70 percent. In July 2018, the Centers for Medicare and Medicaid Services, or CMS, published a final rule permitting further collections and payments to and from certain ACA qualified health plans and health insurance issuers under ACA risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. On December 14, 2018, a Texas U.S. District Court Judge ruled that ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Act. While the Texas U.S. District Court Judge, as well as the Trump administration and CMS, have stated that the ruling will have no immediate effect pending appeal of the decision, it is unclear how this decision, subsequent appeals, and other efforts to repeal and replace ACA will impact ACA.

The Physician Payment Sunshine Act (Sunshine Act), which was enacted as part of ACA, requires covered manufacturers of drugs covered under Medicare, Medicaid or the Children's Health Insurance Program to report annually to the Secretary of the DHHS payments or other transfers of value made by that entity, or by a third party as directed by that entity, to physicians and teaching hospitals, or to third parties on behalf of physicians or teaching hospitals, during the course of the preceding calendar year. The final rule implementing the Sunshine Act, published on February 8, 2013, requires data collection on payments to begin on August 1, 2013. Failure to submit required information may result in significant civil monetary penalties for all payments, transfers of value or ownership or investment interests not reported in an annual submission.

If not preempted by the ACA, several states require pharmaceutical manufacturers to report expenses relating to the marketing and promotion of pharmaceutical products and to report gifts and payments to individual physicians in the states. Other states prohibit providing various other marketing related activities. Still other states require the posting of information relating to clinical studies and their outcomes. In addition, some states, such as California, Nevada and Massachusetts, require pharmaceutical manufacturers to implement compliance programs or marketing codes. Currently, several additional states are considering similar proposals. Compliance with these laws is difficult and time consuming, and companies that do not comply with these state laws face civil penalties.

There has also been increasing legislative and enforcement interest in the United States with respect to drug pricing practices, including several recent Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, increase drug pricing transparency, reduce the cost of drugs under Medicare, review relationships between pricing and manufacturer patient assistance programs, and reform government program drug reimbursement methodologies.

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, the EU provides options for its member states to restrict

the range of medicinal products for which their respective national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products for which we receive marketing approval. Historically, the price structures for products launched in the EU do not follow those of the United States and tend to be significantly lower.

Europe / Rest of World Government Regulation

In addition to regulations in the United States, we and our strategic alliance partners will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of our products.

Whether or not we or our collaborators obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application prior to the commencement of human clinical trials. In the EU, for example, a clinical trial application (CTA), must be submitted to each country's national health authority and an independent ethics committee, much like the FDA and IRB, respectively. Once the CTA is approved in accordance with a country's requirements, the particular clinical trial may proceed.

The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical trials are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

To obtain regulatory approval of an investigational drug or biological product under EU regulatory systems, we or our strategic alliance partners must submit a marketing authorization application. The application used to file the NDA or a Biologics License Application in the United States is similar to the application dossier (eCTD) required in the EU.

For other countries outside of the EU, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, again, the clinical trials are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

If we or our strategic alliance partners fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

EU Review and Approval Process

In the EU, there are two main routes for authorizing the marketing of medicines, a centralized route and a national route. The centralized procedure is compulsory for certain types of medicines, including those that have received orphan designation from the European Commission (Orphan Designation).

Under the centralized authorization procedure, pharmaceutical companies submit a single marketing-authorization application to the EMA. EMA's Committee for Medicinal Products for Human Use (CHMP) carries out a scientific assessment of the application and makes a recommendation to the European Commission whether the medicine should be marketed or not. If authorization is granted by the European Commission, the centralized marketing authorization

is valid in all EU Member States as well as in the European Economic Area (EEA) countries Iceland, Liechtenstein and Norway.

Additionally, medicines that belong to at least one of the below categories may be granted a conditional market authorization (CMA). This regulatory pathway is intended to help speed up patient access to new medicines that are:

- aimed at treating, preventing or diagnosing seriously debilitating or life-threatening diseases;
- intended for use in emergency situations (also less comprehensive pharmaceutical and non-clinical data may be accepted for such products); and/or
- designated as orphan medicines.

A CMA may be granted if: (1) the CHMP finds that the benefit-risk balance of the product is positive, (2) it is likely that the applicant will be able to provide comprehensive data, (3) the unmet medical needs will be fulfilled, and (4) the benefit to public

health of the medicinal product's immediate availability on the market outweighs the risks due to need for further data.

CMAs are valid for one year and can be renewed annually. The CMA holder will be required to complete specific obligations (to complete ongoing or new studies, and in some cases additional activities) with a view to providing comprehensive data confirming that the benefit-risk balance is positive. Once comprehensive data on the product have been obtained, the CMA may be converted into a full marketing authorization (not subject to specific obligations). Initially, this is valid for five years, but can be renewed for unlimited validity.

Orphan Designation in the EU

In order to qualify for Orphan Designation, a medicine must meet the following criteria:

- it must be intended for the treatment, prevention or diagnosis of a disease that is life-threatening or chronically debilitating;
- the prevalence of the condition in the EU must not be more than 5 in 10,000 or it must be unlikely that marketing of the medicine would generate sufficient returns to justify the investment needed for its development; and
- no satisfactory method of diagnosis, prevention or treatment of the condition concerned can be authorized, or, if such a method exists, the medicine must be of significant benefit to those affected by the condition.

EMA is responsible for reviewing applications from sponsors for orphan designation. The EMA's Committee for Orphan Medicinal Products (COMP), through its network of experts, examines applications for Orphan Designation and issues an opinion to EMA. The evaluation process takes approximately of 90 days from validation. Once EMA receives COMP's opinion, EMA sends it to the European Commission, which is responsible for granting the Orphan Designation.

At the time a sponsor of a marketing application files for marketing authorization for a medicine that has received Orphan Designation, the sponsor must also submit a report on the maintenance of the Orphan Designation in parallel. EMA uses this report to determine whether the medicine can maintain its status as an orphan medicine and benefit from the extended market exclusivity applicable to orphan products. Market exclusivity is linked to the maintenance of the Orphan Designation when the medicine receives a marketing authorization for the indication concerned.

If it is determined that a medicine still meets the criteria for Orphan Designation at the time of marketing approval, that medicine may benefit from a period of ten years market exclusivity in the EU. This incentive is intended to protect orphan medicines from market competition with similar medicines with similar indications once they are approved, and fundamentally to encourage the development of medicines for rare diseases.

The applicant is obliged to submit an annual report to the EMA every year after their medicine has been granted orphan designation. The annual report needs provide information on the status of the development of the medicine, such as a review of ongoing clinical studies, a description of the investigation plan for the coming year and any anticipated or current problems in the process, difficulties in testing and potential changes that may have an impact on the medicine's orphan designation.

The European Commission is responsible for granting market exclusivity for orphan medicines. Market exclusivity is linked to each specific Orphan Designation for which a marketing authorization has been granted.

The period of market exclusivity is extended by two years for medicines that also have complied with an agreed pediatric investigation plan (PIP). Each orphan designation for a product linked to a separate orphan condition is eligible for a two-year extension if this is accounted for in the PIP. The extension is granted by the European Commission based on the positive compliance check from the Pediatric Committee and opinion from the CHMP.

Environmental, Health and Safety Regulations

We are subject to various environmental, health and safety regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous substances. From time to time, and in the future, our operations may involve the use of hazardous materials.

Employees

As of December 31, 2018, we had 82 full-time employees. Of these employees, 59 employees are engaged in research and development activities and 23 employees are engaged in marketing, finance, legal, human resources, facilities and general management. We have no collective bargaining agreements with our employees and we have not experienced any work stoppages. We consider our relations with our employees to be good.

Corporate Information

We were incorporated in the State of Delaware in April 2000. Our corporate headquarters are located at 2505 Meridian Parkway, Suite 100, Durham, North Carolina 27713 in a facility we lease encompassing approximately 24,862 square feet of office space. The leases for this facility expire in February 2021. We separately lease laboratory space in Durham and Research Triangle Park, North Carolina, encompassing a total of approximately 10,274 square feet. The leases for this laboratory space in Durham and Research Triangle Park expire in July 2021 and August 2021, respectively.

Our corporate website address is www.chimerix.com. Our filings with the Securities and Exchange Commission are available free of charge through our website as soon as reasonably practicable after being electronically filed with or furnished to the SEC. The information contained on, or that can be accessed through, our website is not part of this Annual Report, and the inclusion of our website address in this Annual Report is an inactive textual reference only.

ITEM 1A. RISK FACTORS

Except for the historical information contained herein or incorporated by reference, this Annual Report and the information incorporated by reference contains forward-looking statements that involve risks and uncertainties. These statements include projections about our research, development and commercialization efforts, our accounting and finances, plans and objectives for the future, future operating and economic performance and other statements regarding future performance. These statements are not guarantees of future performance or events. Our actual results may differ materially from those discussed here. Factors that could cause or contribute to differences in our actual results include those discussed in the following section, as well as those discussed in Part II, Item 7 entitled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and elsewhere throughout this Annual Report and in any other documents incorporated by reference into this Annual Report. You should consider carefully the following risk factors, together with all of the other information included or incorporated in this Annual Report. Each of these risk factors, either alone or taken together, could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our common stock. There may be additional risks that we do not presently know of or that we currently believe are immaterial which could also impair our business and financial position.

An investment in shares of our common stock involves a high degree of risk. You should carefully consider the following information about these risks, together with the other information appearing elsewhere in this Annual Report, before deciding to invest in our common stock. The occurrence of any of the following risks could have a material adverse effect on our business, financial condition, results of operations and future growth prospects. In these circumstances, the market price of our common stock could decline, and you may lose all or part of your investment.

Risks Related To Our Financial Condition and Need For Additional Capital

We have incurred significant losses since our inception. We anticipate that we will continue to incur significant losses for the foreseeable future, and we may never achieve or maintain profitability.

We are a biopharmaceutical company focused primarily on developing our lead product candidate, brincidofovir. We have incurred significant net losses in each year since our inception, including net losses of $69.5 million, $71.0 million and $76.4 million for the twelve months ended December 31, 2018, 2017 and 2016, respectively. As of December 31, 2018, we had an accumulated deficit of approximately $556.3 million.

To date, we have financed our operations primarily through the sale of equity securities and, to a lesser extent, through government funding, licensing fees and debt. We have devoted most of our financial resources to research and

development, including our preclinical development activities and clinical trials. We have not completed development of any product candidates. We expect to continue to incur losses and negative cash flows for the foreseeable future. The size of our losses will depend, in part, on the rate of future expenditures and our ability to generate revenues. In particular, we expect to incur substantial and increased expenses as we seek to:

- continue the development of our lead product candidate, brincidofovir, for the treatment of AdV infection;
- advance the development of an IV formulation of brincidofovir;
- continue the development of brincidofovir for the prevention or treatment of CMV, AdV, BK virus, and other viral indications in HCT recipients, solid organ transplant recipients and other patient populations;
- continue the development of brincidofovir for the treatment of smallpox as a medical countermeasure;
- obtain regulatory approvals for brincidofovir;

- scale-up manufacturing capabilities to commercialize brincidofovir for any indications for which we receive regulatory approval;
- expand our research and development activities and advance our clinical programs;
- maintain, expand and protect our intellectual property portfolio;
- continue our research and development efforts and seek to discover additional product candidates; and
- add operational, financial and management information systems and personnel, including personnel to support our product development and commercialization efforts and operations as a public company.

To become and remain profitable, we must succeed in developing and eventually commercializing products with significant market potential. This will require us to be successful in a range of challenging activities, including discovering product candidates, completing preclinical testing and clinical trials of our product candidates, obtaining regulatory approval for these product candidates, and manufacturing, marketing and selling those products for which we may obtain regulatory approval. We are only in the preliminary stages of some of these activities.

To date, we have not obtained regulatory approval for any of our product candidates, and none of our product candidates have been commercialized. We may never succeed in developing or commercializing any of our product candidates. If our product candidates are not successfully developed or commercialized, or if revenues from any products that do receive regulatory approvals are insufficient, we will not achieve profitability and our business may fail. Even if we successfully obtain regulatory approval to market our product candidates in the United States, our revenues are also dependent upon the size of markets outside of the United States, as well as our ability to obtain market approval and achieve commercial success outside of the United States.

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, expand our business, diversify our product offerings or continue our operations. A decline in the value of our company could cause you to lose all or part of your investment.

Our ability to generate future revenues from product sales is uncertain and depends upon our ability to successfully develop, obtain regulatory approval for, and commercialize our product candidates.

Our ability to generate revenue and achieve profitability depends on our ability, alone or with collaborators, to successfully complete the development, obtain the necessary regulatory approvals and commercialize our product candidates. We do not anticipate generating revenues from sales of our product candidates for the foreseeable future. Our ability to generate future revenues from product sales depends heavily on our success in:

- obtaining favorable results for and advancing the development of brincidofovir and our other product candidates, including successfully completing clinical development of IV and oral formulations of brincidofovir;
- obtaining United States and foreign regulatory approval(s) for brincidofovir;
- launching and commercializing brincidofovir, including establishing a sales force and/or collaborating with third party providers of sales organizations;
- achieving broad market acceptance of brincidofovir in the medical community and with third-party payers;
- delivering a competitive value proposition compared to established competition and/or competitors who will enter the market before or after any of our product candidates, including brincidofovir; and
- generating, licensing or otherwise acquiring a pipeline of product candidates which progress to clinical development, regulatory approval, and commercialization.

Conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data required to obtain regulatory approval and achieve product sales. Our anticipated development costs would likely increase if we do not obtain favorable results or if development

of our product candidates is delayed. In particular, we would likely incur higher costs than we currently anticipate if development of our product candidates is delayed because we are required by the FDA or foreign regulatory authorities to perform studies or trials in addition to those that we currently anticipate, or we decide to conduct additional studies or trials for strategic reasons. For example, in December 2015 we announced that in the SUPPRESS trial brincidofovir did not prevent clinically significant CMV infection through Week 24 after HCT to a greater extent than occurred on placebo, the primary endpoint of the trial. Since that time, we have revised our overall development plan for brincidofovir. We have designed and are conducting multiple trials with the goal of attaining FDA and/or foreign regulatory approval of brincidofovir for commercial indications.

Furthermore, we may have difficulties implementing our clinical trials due to delays in enrollment. For example, enrollment of our AdAPT study and our Phase 2 open label dose-ranging studies of IV BCV in patients with active AdV have faced regulatory and site initiation delays, and we have observed lower than anticipated incidence at the centers that have been initiated, all of which has caused delays in the enrollment of these studies.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to predict with certainty the timing or amount of any increase in our anticipated development costs that will result should any additional trials be necessary.

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 a number of years, if at all. Even if one or more of our product candidates is approved for commercial sale, we anticipate incurring significant costs in connection with commercialization. As a result, we cannot assure you that we will be able to generate revenues from sales of any approved product candidates, or that we will achieve or maintain profitability even if we do generate sales.

If we fail to obtain additional financing, we could be forced to delay, reduce or eliminate our product development programs, seek corporate partners for the development of our product development programs or relinquish or license on unfavorable terms, our rights to technologies or product candidates.

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a time-consuming, expensive and uncertain process that takes years to complete. We believe that our existing capital available to fund operations will enable us to fund our current operating expenses and capital requirements for at least the next twelve months. Based on our 2019 plans for both oral and IV brincidofovir, we currently expect research and development expenses to remain consistent for the full year 2019 as compared to the full year 2018. In addition, we presently continue to provide brincidofovir for the treatment of AdV infection through our expanded access protocol (Study 351) in the US and through the Named Patient Program in the EU. Changing circumstances beyond our control may cause us to consume capital more rapidly than we currently anticipate, and our clinical trials may encounter technical, enrollment or other difficulties that could increase our development costs more than we expected, or because the FDA or foreign regulatory authorities require us to perform studies or trials in addition to those that we currently anticipate. For example, enrollment of our AdAPT study and our Phase 2 open label dose-ranging studies of IV BCV in patients with active AdV have faced regulatory and site initiation delays, and we have observed lower than anticipated incidence at the centers that have been initiated, all of which has caused delays in the enrollment of these studies. We may need to raise additional funds if we choose to initiate clinical trials for our product candidates other than brincidofovir. In any event, we will require additional capital to commercialize our lead product candidate, brincidofovir, which we may obtain through one or more equity offerings, debt financings, government or other third-party funding, strategic alliances and licensing or collaboration arrangements.

Securing additional financing may divert our management from our day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates, including brincidofovir. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. If we are unable to raise additional capital when required or on acceptable terms, we may be required to:

- significantly delay, scale back or discontinue the development or commercialization of our product candidates, including brincidofovir;
- seek corporate partners for brincidofovir or any of our other product candidates at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available; or
- relinquish or license on unfavorable terms, our rights to technologies or product candidates that we otherwise would seek to develop or commercialize ourselves.

If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we will be prevented from pursuing development and commercialization efforts, which will have a material adverse effect on our business, operating results and prospects and on our ability to develop our product candidates.

Risks Related To Clinical Development and Regulatory Approval

We depend on the success of our lead product candidate, brincidofovir, which is still under clinical development, and may not obtain regulatory approval or be successfully commercialized.

We have not marketed, distributed or sold any products. The success of our business depends upon our ability to develop and commercialize our lead product candidate, brincidofovir. In December 2015, we announced that in the SUPPRESS trial, brincidofovir did not prevent clinically significant CMV infection through Week 24 after transplant to a greater extent than occurred on placebo, the primary endpoint of the trial. In addition, overall mortality for brincidofovir and for placebo were not statistically different, but numerically higher for the patients who were randomized to receive brincidofovir.

Our AdVise study of brincidofovir for the treatment of AdV infection in allogeneic HCT recipients and other immunocompromised individuals is complete and did not demonstrate a survival benefit when results were compared to data from Study 305, our historical matched control study.

The AdAPT study is currently enrolling pediatric and young adult allogeneic HCT recipients with AdV infection to compare the average AdV viral burden over 16 weeks in subjects randomized to short-course oral brincidofovir to those who are treated with the local standard-of-care.

Through our continuing development contract with BARDA, we recently completed the in-life segment of our second rabbitpox efficacy study and initiated the pivotal efficacy study in the mouse model (ectromelia virus). We believe that efficacy data from this model could serve as the second animal model to support the approval of brincidofovir for the treatment of smallpox.

There is no guarantee that our current or future clinical trials, including any Phase 3 trials, will be approved by regulators, and no guarantee that they will be completed or, if completed, will be successful, or if successful, will result in an approval for the sale of any of our product candidates. The success of brincidofovir will depend on several factors, including the following:

- successful conduct of required trial(s) of oral brincidofovir for the treatment of adenovirus;
- successful conduct of a second efficacy study of oral brincidofovir in an animal model of smallpox infection, and acceptance of data from these animal model studies by the FDA and foreign regulatory bodies;
- development of an IV formulation and/or alternate drug formulations;
- receipt of marketing approvals from the FDA and corresponding regulatory authorities outside the United States;
- establishing commercial manufacturing capabilities;
- launching commercial sales of the product, whether alone or in collaboration with others;
- acceptance of the product by patients, the medical community and third-party payers;
- effectively competing with other therapies;
- a continued acceptable safety profile of the product following approval;
- obtaining, maintaining, enforcing and defending intellectual property rights and claims; and
- establishing distribution channels in Europe and U.S.

If we do not 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 brincidofovir, which would materially harm our business.

We have never obtained regulatory approval for a drug and we may be unable to obtain, or may be delayed in obtaining, regulatory approval for brincidofovir.

We have never obtained regulatory approval for a drug. It is possible that the FDA and/or foreign health authorities, such as the EMA, may refuse to accept our NDA (or corresponding foreign application) for substantive review or may conclude after review of our data that our application is insufficient to obtain regulatory approval of brincidofovir.

An unfavorable numerical difference in mortality was observed in SUPPRESS and no survival benefit was observed when results from our AdVise study were compared to data from Study 305, our historical matched control study.

The AdAPT study is currently enrolling pediatric and young adult allogeneic HCT recipients with AdV infection to compare the average AdV viral burden over16 weeks in subjects randomized to oral brincidofovir to those who are treated with the local standard-of-care.

We have not yet reached agreement with the FDA or foreign regulators regarding the adequacy of these planned studies with respect to a potential approval for marketing. We may be required to conduct additional clinical, nonclinical or manufacturing validation studies and submit those data before reconsideration of our application occurs. Depending on the extent of these or any other required studies, approval of any NDA or application that we submit may be delayed by several years, or may require us to expend more resources than we have available. It is also possible that additional studies, if performed and completed, may not be considered sufficient by the FDA and/or foreign health authorities to approve our NDA or foreign application.

Through our continuing development contract with BARDA, we recently completed the in-life segment of our second rabbitpox efficacy study and initiated the pivotal efficacy study in the mouse model (ectromelia virus). We believe that efficacy data from this model could serve as the second animal model to support the approval of brincidofovir for the treatment of smallpox.

Any delay in obtaining, or an inability to obtain, regulatory approvals would prevent us from commercializing brincidofovir, generating revenues and achieving and sustaining profitability. If any of these outcomes occur, we may be forced to abandon our

development efforts for brincidofovir, which would have a material adverse effect on our business and could potentially cause us to cease operations.

We depend on the successful completion of animal efficacy studies for brincidofovir for the treatment of smallpox. The positive efficacy results obtained for brincidofovir for the treatment of rabbitpox in the rabbit animal model may not be repeated in future animal efficacy studies.

Before obtaining regulatory approval for brincidofovir for the treatment of smallpox, we must conduct efficacy studies of brincidofovir in animal models of lethal orthopoxvirus infections. These studies are expensive and difficult to design and conduct, can take years to complete, and are uncertain as to outcome. We rely on a limited number of research organizations which conduct orthopoxvirus infection studies. A failure of one or more of our trials can occur at any stage of testing. The outcome of prior efficacy studies of brincidofovir may not be predictive of the success of later animal efficacy studies. Results of these studies are susceptible to varying interpretation.

Through our continuing development contract with BARDA, we recently completed the in-life segment of our second rabbitpox efficacy study and initiated the pivotal efficacy study in the mouse model (ectromelia virus). We believe that efficacy data from this model could serve as the second animal model to support the approval of brincidofovir for the treatment of smallpox. It is our intention to continue development of brincidofovir for the treatment of smallpox through assessment of efficacy in animal models of orthopoxvirus infections.

We depend on the successful completion of clinical trials for our product candidates, including brincidofovir. The positive clinical results obtained for our product candidates in prior clinical studies may not be repeated in future clinical studies.

Before obtaining regulatory approval for the sale of our product candidates, including brincidofovir, we must conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more of our clinical trials can occur at any stage of testing. The outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, 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 for their products.

We may experience a number of unforeseen events during, or as a result of, clinical trials or animal efficacy studies for our product candidates, including brincidofovir, that could adversely affect the completion of our clinical trials, including:

- regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- 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 or abandon product development programs;
- animal efficacy studies of our product candidates may produce negative or inconclusive results, and we may decide, or regulators may require us to conduct additional animal efficacy studies or abandon development programs;
- we might be required to change one of our clinical research organizations (CROs) during ongoing clinical programs;
- the number of subjects required for clinical trials of our product candidates may be larger than we anticipate,
- enrollment in these clinical trials may be insufficient or slower than we anticipate or subjects may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;

- we may have to suspend or terminate clinical trials of our product candidates for various reasons, including a finding that the subjects are being exposed to unacceptable health risks;
- regulators or institutional review boards may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- we may encounter agency or judicial enforcement actions which impact our clinical trials;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate; or
- our product candidates may have undesirable side effects or other unexpected characteristics, causing us or our investigators to suspend or terminate the trials.

An unfavorable numerical difference in mortality was observed in SUPPRESS and no survival benefit was observed when results from our AdVise study were compared to data from Study 305, our historical matched control study.

The AdAPT study is currently enrolling pediatric and young adult allogeneic HCT recipients with AdV infection to compare the average AdV viral burden over 16 weeks in subjects randomized to oral brincidofovir to those who are treated with the local standard-of-care.

We do not know whether any clinical trials we may conduct will demonstrate adequate efficacy and safety to result in regulatory approval to market our product candidates, including brincidofovir. If later stage clinical trials do not produce favorable results, our ability to obtain regulatory approval for our product candidates, including brincidofovir, may be adversely impacted.

We are developing brincidofovir to treat patients who are extremely ill, and patient deaths that occur in our clinical trials could negatively impact our business even if they are not shown to be related to brincidofovir.

It is our intention to further develop our lead product candidate, brincidofovir, for the treatment of AdV infection through clinical trials, and for the prevention or treatment of other DNA viral infections. Many of these patients receive an HCT as a potential cure or remission for many cancers and genetic disorders. For example, patients that were enrolled in AdVise were often extremely sick and had a high likelihood of experiencing adverse outcomes as a result of their infection or due to other significant risks including relapse of their underlying malignancy. To prepare for an HCT, patients receive a pre-transplant conditioning regimen, which involves high-dose chemotherapy and may also include radiation therapy. The conditioning regimen suppresses the patient's immune system in order to prevent it from attacking the new bone marrow.

We are currently assessing the possibility of conducting additional clinical trials for oral or IV brincidofovir for other indications, including in the solid organ transplant setting. In this or other transplant settings, immunosuppressive therapies are administered to decrease the risk of organ rejection and are generally tapered after the first few months; the risk of severe viral infection is highest in the first few months. Generally, patients remain at high risk during the first 100 to 200 days following their transplant and are at increased risk of infections during that period, which can be serious, which may cause loss of the new organ, and which may be life-threatening due to their weakened immune systems.

As a result, it is likely that we will observe severe adverse outcomes during our clinical trials for brincidofovir, including patient death. If a significant number of study subject deaths were to occur, regardless of whether such deaths are attributable to brincidofovir, our ability to obtain regulatory approval and/or achieve commercial acceptance for brincidofovir may be adversely impacted and our business could be materially harmed.

Delays in clinical trials are common and have many causes, and any delay could result in increased costs to us and jeopardize or delay our ability to obtain regulatory approval and commence product sales.

Clinical testing is expensive, difficult to design and implement, can take many years to complete, and is uncertain as to outcome. We may experience delays in clinical trials at any stage of development and testing of our product candidates. Our planned clinical trials may not begin on time, have an effective design, enroll a sufficient number of subjects, or be completed on schedule, if at all.

Events which may result in a delay or unsuccessful completion of clinical trials, including our currently planned or future clinical trials for brincidofovir, include:

- inability to raise funding necessary to initiate or continue a trial;
- delays in obtaining, or failure to obtain, regulatory approval of Investigational New Drug applications or to commence a trial;

- delays in reaching agreement with the FDA and foreign health authorities on final trial design;
- imposition of a clinical hold following an inspection of our clinical trial operations or trial sites by the FDA or other regulatory authorities;
- delays caused by disagreements with existing CROs and/or clinical trial sites;
- delays in reaching agreement on acceptable terms with prospective CROs and clinical trial sites;
- delays in obtaining, or failure to obtain, required IRB or ethics committee (EC) approvals covering each site;
- delays in recruiting suitable patients to participate in a trial;
- delays in having subjects complete participation in a trial or return for post-treatment follow-up;
- delays caused by subjects dropping out of a trial due to side effects or otherwise;
- clinical sites declining to participate or dropping out of a trial to the detriment of enrollment;
- agency or judicial enforcement actions against us;
- time required to add new clinical sites; and
- delays by our contract manufacturers to produce and deliver sufficient supply of clinical trial materials.

Due to the specialized indication and patient populations studied in our past and future clinical trials of brincidofovir, the number of study sites available to us is relatively limited, and therefore enrollment of suitable patients to participate in the trial may take longer than is typical for studies involving other indications. This may result in a delay or unsuccessful completion of our clinical trials. For example, enrollment of our AdAPT study and our Phase 2 open label dose-ranging studies of IV BCV in patients with active AdV have faced regulatory and site initiation delays, and we have observed lower than anticipated incidence at the centers that have been initiated, all of which has caused delays in the enrollment of these studies.

If initiation or completion of any of our clinical trials for our product candidates, including brincidofovir, are delayed for any of the above reasons, our development costs may increase, our approval process could be delayed, any periods during which we may have the exclusive right to commercialize our product candidates may be reduced and our competitors may have more time to bring products to market before we do. Any of these events could impair our ability to generate revenues from product sales and impair our ability to generate regulatory and commercialization milestones and royalties, all of which could have a material adverse effect on our business.

Our product candidates may cause adverse effects or have other properties that could delay or prevent their regulatory approval or limit the scope of any approved label or market acceptance.

Adverse events (AEs) caused by our product candidates could cause us, other reviewing entities, clinical study sites or regulatory authorities to interrupt, delay or halt clinical studies and could result in the denial of regulatory approval. For example, subjects enrolled in our clinical trials for brincidofovir have experienced gastrointestinal AEs and liver-related safety laboratory value changes. In addition, brincidofovir is related to the approved drug cidofovir, a compound which has been shown to result in significant renal toxicity and impairment following use. There is also a risk that our other product candidates may induce AEs, many of which may be unknown at this time. If an unacceptable frequency and/or severity of AEs are reported in our clinical trials for our product candidates, our ability to obtain regulatory approval for product candidates, including brincidofovir, may be negatively impacted. We anticipate that we will need to conduct one or more additional clinical trials in order to attain FDA and/or foreign regulatory approval of brincidofovir.

If any of our approved products cause serious or unexpected side effects prior to or after receiving market approval, a number of potentially significant negative consequences could result, including:

- regulatory authorities may approve the product only with a REMS, potentially with restrictions on distribution and other elements to assure safe use (ETASU);
- regulatory authorities may withdraw their approval of the product or impose restrictions on its distribution in a form of a modified REMS;
- regulatory authorities may require the addition of labeling statements, such as warnings or contraindications;
- we may be required to change the way the product is administered or to conduct additional clinical studies;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected product candidate and could substantially increase the costs of commercializing our product candidates.

After the completion of our clinical trials, we cannot predict whether or when we will obtain regulatory approval to commercialize brincidofovir and we cannot, therefore, predict the timing of any future revenue from brincidofovir.

We cannot commercialize our product candidates, including brincidofovir, until the appropriate regulatory authorities have reviewed and approved the product candidate. The regulatory agencies may not complete their review processes

in a timely manner, or we may not be able to obtain regulatory approval for brincidofovir. Additional delays in the United States may result if brincidofovir is brought before an FDA advisory committee, which could recommend restrictions on approval or recommend non-approval of the product candidate. In the EU context, an Oral Explanation during MAA review could extend approval timelines and result in a Negative Opinion. A re-examination procedure is available in the EU whereby a Negative Opinion could be over-turned and become a Positive Opinion. New rapporteurs would be selected for the product. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory agency policy during the period of product development, clinical studies and the review process. As a result, we cannot predict when, if at all, we will receive any future revenue from commercialization of any of our product candidates, including brincidofovir.

Even if we obtain regulatory approval for brincidofovir and our other product candidates, we will still face extensive regulatory requirements and our products may face future development and regulatory difficulties.

Even if we obtain regulatory approval, the granting authority may still impose significant restrictions on the indicated uses,

distribution or marketing of our product candidates, including brincidofovir, or impose ongoing requirements for potentially costly post-approval studies or post-market surveillance. For example, the labeling ultimately approved for our product candidates, including brincidofovir, will likely include restrictions on use due to the specific patient population and manner of use in which the drug was evaluated and the safety and efficacy data obtained in those evaluations. In addition, the distribution of brincidofovir may be tightly controlled through a REMS with ETASU, which are required medical interventions or other actions healthcare professionals need to execute prior to prescribing or dispensing the drug to the patient. Some actions may also be required in order for the patient to continue on treatment. In addition, the label for brincidofovir may be required to include a boxed warning, or "black box," regarding brincidofovir being carcinogenic, teratogenic and impairing fertility in animal studies, as well as a contraindication in patients who have had a demonstrated clinically significant hypersensitivity reaction to brincidofovir or cidofovir or any component of the formulation. The brincidofovir labeling may also include warnings or black boxes pertaining to gastrointestinal AEs or liver-related safety laboratory value changes.

Brincidofovir and our other product candidates will also be subject to additional ongoing regulatory requirements governing the labeling, packaging, storage, distribution, safety surveillance, advertising, promotion, record-keeping and reporting of safety and other post-market information. In the United States, the holder of an approved NDA is obligated to monitor and report AEs and any failure of a product to meet the specifications in the NDA. The holder of an approved NDA must also submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. If a REMS is required, the NDA holder may be required to monitor and evaluate those in the healthcare system who are responsible for implementing ETASU measures. Advertising and promotional materials must comply with FDA rules and are subject to FDA review, in addition to other potentially applicable federal and state laws. Moreover, EU and member countries impose strict restrictions on the promotion and marketing of drug products. The off-label promotion of medicinal products is prohibited in the U.S., EU and in other territories. The promotion of medicinal products that are not subject to a marketing authorization is also prohibited in the EU. Violations of the rules governing the promotion of medicinal products in the EU and in other territories could be penalized by administrative measures, fines and imprisonment.

In addition, manufacturers of drug products and their facilities are subject to payment of user fees and continual review and periodic inspections by regulatory authorities for compliance with cGMP, and adherence to commitments made in the application. If we, or a regulatory agency, discover previously unknown problems with a product, such as quality issues or AEs of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions relative to that product or the manufacturing facility, including requiring recall or withdrawal of the product from the market or suspension of manufacturing.

If we fail to comply with applicable regulatory requirements following approval of our product candidate, a regulatory agency may:

- issue an untitled or warning letter asserting that we are in violation of the law;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve a pending application or supplements to an application submitted by us;
- recall and/or seize product; or
- refuse to allow us to enter into supply contracts, including government contracts.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize brincidofovir and our other product candidates and inhibit our ability to generate revenues.

Obtaining FDA approval for brincidofovir or any of our other products in the United States does not mean we will ever obtain approval for or commercialize brincidofovir or any of our other products outside of the United States, nor does approval of brincidofovir or any of our other products outside the United States mean we will ever obtain approval for or commercialize brincidofovir or any of our other products inside the United States, all of which could limit our ability to realize their full market potential.

In order to market any products outside of the United States, 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 does not ensure approval by regulatory authorities in other countries or jurisdictions. 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 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 international markets, and we do not have experience in obtaining regulatory approval in any 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 our products will be unrealized.

Conversely, approval by regulatory authorities outside the United States, such as the European Commission, does not ensure approval by the FDA. Moreover, clinical trials conducted outside the United States may not be accepted by the FDA.

There is no guarantee that brincidofovir or any other of our product candidates will be eligible for or receive certain regulatory incentives, such as orphan drug designation, and even if they do, we may never actually realize some or all of the associated benefits, such as market exclusivity.

There are a variety of incentives made available by regulatory authorities in the United States, the EU, and other countries, such as orphan drug designation, which may benefit companies developing medicines in areas of unmet need. There is no guarantee, however, that brincidofovir or any of our other product candidates will be eligible for or receive such incentives. For example, even though the Company has received orphan designation for brincidofovir in the EU for the treatment of AdV in immunocompromised patients, prevention of CMV disease, and treatment of smallpox, the European Commission must determine that brincidofovir still meets the mandatory criteria for each of these orphan designations at the time of marketing approval, which may not happen.

Our relationships with investigators, health care professionals, consultants, third-party payers, and customers may be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and others play a primary role in the recommendation and prescribing of any products for which we obtain marketing approval. Our current business operations and future arrangements with investigators, healthcare professionals, consultants, third-party payers and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations. These laws may constrain the business or financial arrangements and relationships through which we research, market, sell and distribute our products for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations, include, but are not limited to, the following:

- the federal healthcare anti-kickback statute which prohibits, among other things, persons or entities from knowingly and willfully soliciting, offering, receiving or paying remuneration (including any kickback, bribe or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under federal healthcare programs such as Medicare and Medicaid;
- the federal civil and criminal false claims laws and the Federal Civil Monetary Penalties Act, including the Federal Civil False Claims Act (False Claims Act) which permit private individuals to bring a civil action on behalf of the federal government to enforce certain of these laws thought civil whistleblower or qui tam actions, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, to the federal government, claims for payment or approval that are false or fraudulent or from knowingly making a false statement to improperly avoid, decrease or conceal an obligation to pay money to the federal government;
-

the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA) which, among other things, imposes criminal liability for knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or to obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payer (e.g., public or private) and knowingly or willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statement in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act (HITECH) and their implementing regulations, and as amended again by the final HIPAA omnibus rule, Modifications to the HIPAA Privacy, Security, Enforcement, and Breach Notification Rules Under HITECH and the Genetic Information Nondiscrimination Act; Other Modifications to HIPAA, published in January 2013, which imposes certain obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information without appropriate authorization by entities subject to the rule, such as health plans, healthcare clearinghouses and certain healthcare providers, as well as their business associates;
- the General Data Protection Regulation (GDPR), which impose obligations on companies in relation to the handling of personal data of individuals within the EU, along with related national legislation;

- mandated physician payments reporting laws and/or requirements throughout global jurisdictions, including EU member states, in which we conduct research and development and/or other business activities;
- the FDCA which prohibits, among other things, the adulteration or misbranding of drugs and devices;
- the federal transparency law, enacted as part of the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the ACA), and its implementing regulations, which requires manufacturers of drugs, devices, biologicals and medical supplies to report to the Centers for Medicare & Medicaid Services (CMS) information related to payments and other transfers of value made to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and
- analogous state laws and regulations, including: state anti-kickback and false claims laws, which may apply to our business practices, including but not limited to, research, distribution, sales and marketing arrangements and claims involving healthcare items or services reimbursed by state governmental and non-governmental third-party payers, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government; state and local laws that require the registration of pharmaceutical sales representatives; state laws and regulations that require manufacturers to file reports relating to pricing and marketing information, which requires tracking gifts and other remuneration and items of value provided to healthcare professionals and entities; and state laws governing the privacy and security of health information, many of which differ from each other in significant ways and often are not preempted by HIPAA.

Efforts to ensure that our business arrangements with third parties comply with applicable healthcare laws and regulations involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance 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 or any other health regulatory 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, additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our financial results. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and/or divert our management's attention from the operation of our business. If any of the physicians or other providers or entities with whom we expect to do business are found to be not in compliance with applicable laws, they also may be subject to criminal, civil or administrative sanctions, including, but not limited to, exclusions from government funded healthcare programs, which could also materially affect our business.

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

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any products for which we obtain marketing approval.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (Medicare Modernization Act) changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician-administered drugs. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class. Cost reduction initiatives and other

provisions of this legislation could decrease the coverage and price that we receive for any approved products. While the Medicare Modernization Act applies only to drug benefits for Medicare beneficiaries, private payers often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the Medicare Modernization Act may result in a similar reduction in payments from private payers.

More recently, in March 2010, the ACA was enacted to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for health care and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. The ACA revises the definition of “average manufacturer price” for reporting purposes, which could increase the amount of Medicaid drug rebates to states. Further, the new law imposes a significant annual fee on companies that manufacture or import branded prescription drug products. New provisions affecting compliance have also been enacted, which may affect our business practices with health care practitioners. However, there have been judicial and Congressional challenges to certain aspects of the ACA, as well as recent efforts by the Trump administration to repeal and replace certain aspects of the ACA, and we expect such challenges to continue. Since January 2017, President Trump has signed two Executive Orders and other directives designed to delay the implementation

of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the ACA have been enacted. The Tax Cuts and Jobs Act of 2017 (Tax Act) includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." On January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain fees mandated by the ACA, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. The Bipartisan Budget Act of 2018, or the BBA, among other things, amended the ACA, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, and also increases in 2019 the percentage that a drug manufacturer must discount the cost of prescription drugs from 50 percent to 70 percent. In July 2018, CMS published a final rule permitting further collection and payments to and from certain ACA qualified health plans and health insurance issuers under the ACA risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. On December 14, 2018, a Texas U.S. District Court Judge ruled that ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Act. While the Texas U.S. District Court Judge, as well as the Trump administration and CMS, have stated that the ruling will have no immediate effect pending appeal of the decision, it is unclear how this decision, subsequent appeals, and other efforts to repeal and replace ACA will impact ACA and our business. Congress also could consider additional legislation to repeal or repeal and replace other elements of the ACA.

Although it is too early to determine the full effect of the ACA, the law appears likely to continue the pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs.

Legislative and regulatory proposals have also been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products.

Additionally, there has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At the federal level, the Trump administration's budget proposal for fiscal year 2019 contains additional drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid and to eliminate cost sharing for generic drugs for low-income patients. Further, the Trump administration released a "Blueprint" to lower drug prices and reduce out-of-pocket costs of drugs. This "Blueprint" contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out-of-pocket costs of drug products paid by consumers. The U.S. Department of Health and Human Services (DHHS) has already started the process of soliciting feedback on some of these measures and, at the same time, is immediately implementing other measures under its existing authority. For example, in September 2018, CMS announced that it will allow Medicare Advantage Plans the option to use step therapy for Part B drugs beginning January 1, 2019, and in October 2018, CMS proposed a new rule that would require direct-to-consumer television advertisements of prescription drugs and biological products, for which payment is available through or under Medicare or Medicaid, to include in the advertisement the Wholesale Acquisition Cost, or list price, of that drug or biological product. On January 31, 2019, the DHHS Office of Inspector General proposed modifications to federal Anti-Kickback Statute

safe harbors which, among other things, may affect rebates paid by manufacturers to Medicare Part D plans, the purpose of which is to further reduce the cost of drug products to consumers. Although a number of these, and other potential, proposals will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

Further, on May 30, 2018, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017 (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 I 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.

Healthcare reform measures that may be adopted in the future may result in more rigorous coverage criteria, lower reimbursement, and additional downward pressure on the price that we receive for any future approved product. We cannot predict what healthcare reform initiatives may be adopted in the future.

Risks Related to Our Reliance on Third Parties

We rely on third-party manufacturers to produce our preclinical and clinical drug supplies, and we intend to rely on third parties to produce commercial supplies of any approved product candidates.

We do not own or operate, and we do not expect to own or operate, facilities for product manufacturing, storage and distribution, or testing. In the past, we have relied on third-party manufacturers for supply of our preclinical and clinical drug supplies. We expect that in the future we will continue to rely on such manufacturers for drug supply that will be used in clinical trials of our product candidates, including brincidofovir, and for commercialization of any of our product candidates that receive regulatory approval.

Our reliance on third-party manufacturers entails risks, including:

- inability to meet our product specifications and quality requirements consistently;
- delay or inability to procure or expand sufficient manufacturing capacity;
- manufacturing and product quality issues related to scale-up of manufacturing;
- costs and validation of new equipment and facilities required for scale-up;
- failure to comply with cGMP and similar foreign standards;
- inability to negotiate manufacturing agreements with third parties under commercially reasonable terms;
- termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us;
- reliance on a limited number of sources, and in some cases, single sources for product components, such that if we are unable to secure a sufficient supply of these product components, we will be unable to manufacture and sell our product candidates in a timely fashion, in sufficient quantities or under acceptable terms;
- lack of qualified backup suppliers for those components that are currently purchased from a sole or single source supplier;
- operations of our third-party manufacturers or suppliers could be disrupted by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier;
- carrier disruptions or increased costs that are beyond our control; and
- failure to deliver our products under specified storage conditions and in a timely manner.

Any of these events could lead to clinical study delays, failure to obtain regulatory approval or impact our ability to successfully commercialize our products. Some of these events could be the basis for FDA or equivalent foreign regulator action, including injunction, recall, seizure, or total or partial suspension of production.

We rely on limited sources of supply for the drug component for our lead product candidate, brincidofovir, and any disruption in the chain of supply may cause delay in developing and commercializing brincidofovir.

Manufacturing of drug components is subject to certain FDA and comparable foreign qualifications with respect to manufacturing standards. We are currently validating the drug substance manufacturing process at our selected contractor that will produce the commercial supply of drug substance and have selected commercial tablet and suspension manufacturers to optimize tablet and suspension formulation production to meet forecasted commercial demand. There can be no assurance that such transfer to the selected vendors will be successful. It is our expectation that only one supplier of drug substance and one supplier of drug product will be qualified as vendors with the FDA. If supply from an approved vendor is interrupted, there could be a significant disruption in commercial supply of

brincidofovir. An alternative vendor would need to be qualified through an NDA supplement which could result in further delay. The FDA or other regulatory agencies outside of the United States may also require additional studies if a new drug substance or drug product supplier is relied upon for commercial production.

These factors could cause the delay of clinical trials, regulatory submissions, required approvals or commercialization of brincidofovir, and cause us to incur additional costs. Furthermore, if our suppliers fail to deliver the required commercial quantities of active pharmaceutical ingredient on a timely basis and at commercially reasonable prices, and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical trials for brincidofovir may be delayed, which could inhibit our ability to generate revenues.

Manufacturing issues may arise that could increase product and regulatory approval costs or delay commercialization of brincidofovir.

We have a validated process for drug substance production for brincidofovir at a scale that is well in excess of our anticipated commercial scale. We are currently revalidating our drug substance process, and will begin revalidating our drug product processes, using our current commercial processes at our intended commercial scale with our intended commercial manufacturers.

The validation processes, along with ongoing stability studies and analyses we are conducting, may reveal difficulties in our processes which could require resolution in order to proceed with our planned clinical trials and obtain regulatory approval for the commercial marketing of brincidofovir. In the future, we may identify significant impurities, which could result in increased scrutiny by the regulatory agencies, delays in clinical program and regulatory approval for brincidofovir, increases in our operating expenses, or failure to obtain or maintain approval for brincidofovir.

We depend on the continuation of our current collaboration with ContraVir Pharmaceuticals, who is currently responsible for developing and commercializing CMX157.

In 2014, we entered into a licensing arrangement with ContraVir, whereby ContraVir is responsible for the future development and commercialization of CMX157. Under this arrangement, ContraVir is responsible for conducting preclinical studies and clinical trials, obtaining required regulatory approvals for CMX157, and manufacturing and commercializing CMX157. Our right to receive milestone and royalty payments under the licensing agreement depends on the achievement of certain development, regulatory and commercial milestones by ContraVir.

The development and commercialization of CMX157 and our ability to receive potential milestones and royalty payments under the license agreement with ContraVir, would be adversely affected if ContraVir:

- lacks or does not devote sufficient time and resources to the development and commercialization of CMX157;
- lacks or does not devote sufficient capital to fund the development and commercialization of CMX157;
- develops, either alone or with others, products that compete with CMX157;
- fails to gain the requisite regulatory approvals for CMX157;
- does not successfully commercialize CMX157;
- does not conduct its activities in a timely manner;
- terminates its license with us;
- does not effectively pursue and enforce intellectual property rights relating to CMX157; or
- merges with a third-party that wants to terminate the collaboration.

We have limited or no control over the occurrence of any of the foregoing. Furthermore, disagreements with ContraVir could lead to litigation or arbitration, which could be time-consuming and expensive. If any of these issues arise, it may delay the development and commercialization milestones and royalties based on further development and sales of CMX157.

We rely on third parties to conduct, supervise and monitor our clinical studies and related data, and if those third parties perform in an unsatisfactory manner, it may harm our business.

We rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials. While we have agreements governing their activities, we have limited influence over their actual performance. We have relied and plan to continue to rely upon CROs to monitor and manage data for our ongoing clinical programs for brincidofovir and our other product candidates, as well as the execution of nonclinical studies. We control only certain aspects of

our CROs' activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards and our reliance on CROs does not relieve us of our regulatory responsibilities.

We and our CROs are required to comply with the FDA's guidance for clinical trials conducted within the jurisdiction of the United States (or the foreign regulatory authority equivalent for clinical trials conducted outside the jurisdiction of the United States), which follows the International Council for Harmonization Good Clinical Practice (ICH GCP), which are regulations and guidelines enforced by the FDA for all of our product candidates in clinical development. The FDA enforces the ICH GCP through periodic inspections of trial sponsors, principal investigators and clinical trial sites. If we or our CROs fail to comply with the ICH GCP, the clinical data generated in our clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving our marketing applications. In addition, our Phase 3 clinical trials for brincidofovir will require a sufficiently large number of test subjects to evaluate the safety and effectiveness of brincidofovir. Accordingly, if our CROs fail to comply with these regulations or fail to recruit a sufficient number of subjects, we may be required to repeat these Phase 3 clinical trials, which would delay the regulatory approval process.

Our CROs are not our employees, and we cannot control whether or not they devote sufficient time and resources to our ongoing clinical and nonclinical programs. These CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical studies, or other drug development activities which could harm our competitive position. We face the risk of potential unauthorized disclosure or misappropriation of our intellectual property by CROs, which may reduce our trade secret protection and allow our potential competitors to access and exploit our proprietary technology.

If our CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for any other reasons, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize brincidofovir or our other product candidates. Disagreements with our CROs over contractual issues, including performance, compliance or compensation could lead to termination of CRO agreements and/or delays in our clinical program and risks to the accuracy and usability of clinical data. As a result, our financial results and the commercial prospects for brincidofovir and any other product candidates that we develop would be harmed, our costs could increase, and our ability to generate revenues could be delayed.

Risks Related to Commercialization of Our Product Candidates

The commercial success of brincidofovir and our other product candidates will depend upon the acceptance of these products by the medical community, including physicians, patients, pharmacists and health care payers.

If any of our product candidates, including brincidofovir, receive marketing approval, they may nonetheless not gain sufficient market acceptance by physicians, patients, healthcare payers and others in the medical community. If these products do not achieve an adequate level of market acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of any of our product candidates, including brincidofovir, will depend on a number of factors, including:

- demonstration of clinical safety and efficacy in our clinical trials;
- relative convenience, ease of administration and acceptance by physicians, patients, pharmacists and health care payers;
- prevalence and severity of any AEs;
- limitations or warnings contained in the FDA-approved labeling from Regulatory Authorities such as the FDA and EMA for the relevant product candidate;
- availability, efficacy and safety of alternative treatments;
- price and cost-effectiveness;
- effectiveness of our or any future collaborators' or competitor's sales and marketing strategies;
- ability to obtain hospital formulary approval;
- ability to ensure availability for product through appropriate channels;
- ability to maintain adequate inventory; and
- ability to obtain and maintain sufficient third-party coverage and adequate reimbursement, which may vary from country to country.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may be unable to generate any revenue.

We currently do not have an organization for the sales and distribution of pharmaceutical products. The cost of establishing and maintaining such an organization may exceed the cost-effectiveness of doing so. In order to market any products that may be approved, including brincidofovir, we must establish our sales, marketing, managerial and

other non-technical capabilities or make arrangements with third parties to perform these services. We may enter into strategic partnerships with third parties to commercialize our product candidates, including brincidofovir.

Our strategy for brincidofovir is to establish a specialty sales force and/or collaborate with third parties to promote the product to healthcare professionals and third-party payers in the United States and elsewhere. We may elect to launch with a contract sales organization and utilize accompanying commercial support services provided by a contract sales organization. Our future collaboration partners, if any, may not dedicate sufficient resources to the commercialization of our product candidates or may otherwise fail in their commercialization due to factors beyond our control. If we are unable to establish effective collaborations to enable the distribution and sale of our product candidates to healthcare professionals and in geographical regions, including the United States, that are not covered by our own marketing and sales force, or if our potential future collaboration partners do not successfully commercialize our product candidates, our ability to generate revenues from product sales, including sales of brincidofovir, will be adversely affected.

Establishing an internal or contract sales force involves many challenges, including:

- recruiting and retaining talented people;
- training employees that we recruit;
- establishing compliance standards;
- setting the appropriate system of incentives;
- managing additional headcount;
- ensuring that appropriate support functions are in place to support sales force organizational needs; and
- integrating a new business unit into an existing corporate architecture.

If we are unable to establish our own sales force or negotiate a strategic partnership for the commercialization of brincidofovir in any markets, we may be forced to delay the potential commercialization of brincidofovir in those markets, reduce the scope of our sales or marketing activities for brincidofovir in those markets or undertake the commercialization activities for brincidofovir in those markets at our own expense. If we elect to increase our expenditures to fund commercialization activities ourselves, we will need to obtain additional capital, which may not be available to us on acceptable terms, or at all. If we do not have sufficient funds, we will not be able to bring brincidofovir to market or generate product revenue. Limited or lack of funding will impede our ability to achieve successful commercialization.

If we are unable to establish adequate sales, marketing and distribution capabilities, whether independently or with third parties, we may not be able to generate sufficient product revenue and may not become profitable. We will be competing with many companies that currently have extensive and well-funded marketing and sales operations. Without an internal team or the support of a third party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies.

In addition, there are risks involved with both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time-consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales, marketing and market access personnel.

If we obtain approval to commercialize any products outside of the United States, a variety of risks associated with international operations could materially adversely affect our business.

If our product candidates are approved for commercialization, we may enter into agreements with third parties to market those product candidates outside the United States, including brincidofovir. We expect that we will be subject to additional risks related to entering into international business relationships, including:

- different regulatory requirements for drug approvals in the EU and other foreign countries;
- reduced protection for intellectual property rights;
- unexpected changes in tariffs, trade barriers and regulatory and labor requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- differing payer reimbursement regimes, governmental payers or patient self-pay systems and price controls;

- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad;
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires; and
- regulatory and compliance risks that relate to maintaining accurate information and control over activities that may fall within the purview of the U.S. Foreign Corrupt Practices Act, its books and records provisions or its anti bribery provisions, or similar anti bribery or anti corruption laws and regulations.

We have limited experience in these areas. In addition, there are complex regulatory, tax, labor and other legal requirements imposed by both the EU and many of the individual countries in Europe with which we will need to comply. Many U.S.-based biopharmaceutical companies have found the process of marketing their own products outside the United States to be very challenging.

We face significant competition from other biotechnology and pharmaceutical companies and our operating results will suffer if we fail to compete effectively.

The biotechnology and pharmaceutical industries are intensely competitive. We have competitors both in the United States and internationally, including major multinational pharmaceutical companies, biotechnology companies and universities and other research institutions.

Based on market research, competing products that are currently used to prevent or treat AdV and/or CMV include and are not limited to:

- cidofovir, a drug that is sold by generic manufacturers;
- oral and intravenous ganciclovir, a drug that is sold by generic manufacturers;
- Valcyte® (valganciclovir), a prodrug of ganciclovir that is marketed by Genentech, Inc. and generic manufacturers;
- foscarnet sodium for injection available through generic manufacturers;
- acyclovir, a drug that is sold by generic manufacturers; and
- Prevymis® (letermovir), an anti-CMV drug marketed by Merck & Co., Inc.

Other product candidates currently in development or under regulatory review may compete against brincidofovir for the prevention or mitigation of AdV and/or CMV infection in a variety of settings, including:

- maribavir (SHP620) from Shire for CMV infections in transplant recipients; and
- patient-specific T-cell therapies directed at antigens of CMV and other DNA viruses, including AdV.

Many of our competitors have substantially greater financial, technical, commercial and other resources, such as larger research and development staff, stronger intellectual property portfolios and experienced marketing and manufacturing organizations and established sales forces. Additional mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors.

Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring or licensing, on an exclusive basis, drug products that are more effective or less costly than brincidofovir or any other drug candidate that we are currently developing or that we may develop.

We will face competition from other drugs currently approved or that will be approved in the future for the same indications. Therefore, our ability to compete successfully will depend largely on our ability to:

- discover and develop medicines that are superior to other products in the market;
- demonstrate through our clinical trials that our product candidates, including brincidofovir, are differentiated from existing and future therapies;
- evaluate new potential indications across the lifecycle of brincidofovir;
- attract qualified scientific, product development and commercial personnel;
- obtain and successfully defend and enforce patent and/or other proprietary protection for our medicines and technologies;
- obtain required regulatory approvals;
- successfully collaborate with pharmaceutical companies in the discovery, development and commercialization of new medicines;
- deliver a competitive value proposition compared to established competition and/or competitors who will enter the market before or after any of our product candidates, including brincidofovir; and
-

negotiate competitive pricing and reimbursement with third-party payers.

The availability of our competitors' products could limit the demand, and the price we are able to charge, for brincidofovir and any other product candidate we develop. We will not achieve our business plan if the acceptance of brincidofovir is inhibited by price competition or reimbursement issues or the reluctance of physicians to switch from existing drug products to brincidofovir, or if physicians switch to other new drug products or choose to reserve brincidofovir for use in limited circumstances. The inability to compete with existing or subsequently introduced drug products would have a material adverse impact on our business, financial condition and prospects.

Established pharmaceutical companies may invest heavily to accelerate discovery and development of novel compounds or to in-license novel compounds that could make our product candidates, including brincidofovir, less competitive. In addition, any new product that competes with an approved product must demonstrate compelling advantages in efficacy, convenience, tolerability

and safety in order to overcome price competition and to be commercially successful. Accordingly, our competitors may succeed in obtaining patent protection, receiving FDA approval or discovering, developing and commercializing medicines before we do, which would have a material adverse impact on our business.

New technologies or procedures could be developed that would change or restrict the number of patients undergoing hematopoietic cell or solid organ transplants. A reduction in the number of transplants could negatively impact our commercial business by decreasing sales of our products and limiting peak sales potential.

Hospital formulary approval and reimbursement may not be available for brincidofovir and our other product candidates, which could make it difficult for us to sell our products profitably.

Obtaining hospital formulary approval can be an expensive and time-consuming process. We cannot be certain if and when we will obtain formulary approval to allow us to sell our product candidates, including brincidofovir, into our target markets. Failure to obtain timely formulary approval will limit our commercial success.

Furthermore, market acceptance and sales of brincidofovir, or any other product candidates that we develop, will depend in part on the extent to which coverage and reimbursement for these products and related treatments will be available from third-party payers such as government health administration authorities, private health insurers and other organizations. Third-party payers decide which drugs they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Third-party payers have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Obtaining reimbursement for our products may be particularly difficult because of the higher prices often associated with products administered under the supervision of a physician. We cannot be sure that reimbursement will be available for brincidofovir, or any other product candidates.

Also, reimbursement amounts may reduce the demand for, or the price of, our products. If reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize brincidofovir, or any other product candidates that we develop.

There have been a number of legislative and regulatory proposals to change the healthcare system in the United States and in some foreign jurisdictions that could affect our ability to sell any future products profitably. These legislative and regulatory changes may negatively impact the reimbursement for any future products, following approval. The availability of generic treatments may also substantially reduce the likelihood of reimbursement for any future products, including brincidofovir. The application of user fees to generic drug products will likely expedite the approval of additional generic drug treatments. We expect to experience pricing pressures in connection with the sale of brincidofovir and any other product candidate that we develop, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. In addition, there may be significant delays in obtaining reimbursement for approved products, and coverage may be more limited than the purposes for which the product is approved by the FDA or regulatory authorities in other countries. Moreover, eligibility for reimbursement does not imply that any product will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim payments for new products, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Payment rates may vary according to the use of the product and the clinical setting in which it is used, may be based on payments allowed for lower cost products that are already reimbursed, and may be incorporated into existing payments for other services. Net prices for products may be reduced by mandatory discounts or rebates required by government healthcare programs or private payers and by any future relaxation of laws that presently restrict imports of products from countries where they may be sold at lower prices than in the United States. Third-party payers often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies, but also have their own methods and approval process apart from Medicare determinations. Therefore, one third-party payer's

determination to provide coverage for a product does not assure that other payers will also provide coverage for the product.

Our inability to promptly obtain coverage and profitable payment rates from both government funded and private payers for any of our product candidates, including brincidofovir, could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

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.

The success of our business depends primarily upon our ability to identify, develop and commercialize product candidates. Because we have limited financial and managerial resources, we focus on research programs and product candidates for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or other indications that later prove to have greater commercial potential.

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:

- our research methodology or that of our collaboration partners may be unsuccessful in identifying potential product candidates;
- our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval; and
- our collaboration partners may change their development profiles for potential product candidates or abandon a therapeutic area.

If any of these events occur, we may be forced to abandon our development efforts for a program or programs, which would have a material adverse effect on our business and could potentially cause us to cease operations. Research programs to identify new product candidates require substantial technical, financial and human resources. We may focus our research efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful.

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 advantageous for us to retain sole development and commercialization rights.

Risks Related to Our Intellectual Property

If we are unable to obtain or protect intellectual property rights related to our products and product candidates, 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 the intellectual property related to our products and product candidates. The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own or in-license may fail to result in issued patents with claims that cover the products in the United States or in other countries. If this were to occur, early generic competition could be expected against brincidofovir and any other product candidates in development. There is no assurance that all of the potentially relevant prior art relating to our patents and patent applications has been found, which can invalidate a patent or prevent a patent from issuing based on a pending patent application. Even if patents do successfully issue, third parties may challenge their validity, enforceability, scope or ownership, which may result in such patents, or our rights to such patents, being narrowed or invalidated.

Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property or prevent others from designing around our claims. If the patent applications we hold or license with respect to brincidofovir fail to issue or if their breadth or strength of protection is threatened, it could dissuade companies from collaborating with us to develop, and threaten our ability to commercialize, our products. We cannot offer any assurances about which, if any, patents will issue or whether any issued patents will be found not invalid and not unenforceable, will go unthreatened by third parties or will adequately protect our products and product candidates. Further, if we encounter delays in regulatory approvals, the period of time during which we could market brincidofovir under patent protection could be reduced. Since patent applications in the United States and most other countries are confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we or our licensors were the first to file any patent application related to brincidofovir or our other product candidates. Furthermore, if third parties have filed such patent applications, an interference proceeding in the United States can be provoked by a third party or instituted by us to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. An unfavorable outcome could require us to cease using the related

technology or to attempt to license it from the prevailing party, which may not be possible. In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable, processes for which patents are difficult to enforce and other elements of our drug discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. Although we expect all of our employees to assign their inventions to us, and all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information or technology to enter into confidentiality agreements, we cannot provide any assurances that all such agreements have been duly executed, that such agreements provide adequate protection and will not be breached, that our trade secrets and other confidential proprietary information will not otherwise be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. If we are unable to prevent material disclosure of the non-patented intellectual property related to our technologies to third parties, and there is no guarantee that we will have any such enforceable trade secret protection, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations and financial condition.

Further, the laws of some foreign countries do not protect patents and other proprietary rights to the same extent or in the same

manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property abroad. We may also fail to pursue or obtain patents and other intellectual property protection relating to our products and product candidates in all foreign countries.

Finally, certain of our activities and our licensors' activities have been funded, and may in the future be funded, by the U.S. federal government. When new technologies are developed with U.S. federal government funding, the government obtains certain rights in any resulting patents, including a nonexclusive license authorizing the government to use the invention for non-commercial purposes. These rights may permit the government to disclose our confidential information to third parties and to exercise "march-in" rights to use or allow third parties to use our patented technology. The government can exercise its march-in rights if it determines that action is necessary because we fail to achieve practical application of the U.S. government-funded technology, because action is necessary to alleviate health or safety needs, to meet requirements of federal regulations or to give preference to U.S. industry. In addition, U.S. government-funded inventions must be reported to the government, U.S. government funding must be disclosed in any resulting patent applications, and our rights in such inventions may be subject to certain requirements to manufacture products in the United States.

Third-party claims of intellectual property infringement may prevent or delay our development and commercialization efforts or otherwise affect our business.

Our commercial success depends in part on our avoiding infringement and other violations of the patents and proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions and inter party reexamination proceedings before the United States Patent and Trademark Office (U.S. PTO) and its foreign counterparts. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we and our collaborators are developing product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, and as we gain greater visibility and market exposure as a public company, the risk increases that our product candidates or other business activities may be subject to claims of infringement of the patent and other proprietary rights of third parties. Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of brincidofovir and/or our other product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our product candidates, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, or until such patents expire.

Similarly, if any third-party patent were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or methods of use, including combination therapy, the holders of any such patent may be able to block our ability to develop and commercialize the applicable product candidate unless we obtained a license or until such patent expires. In either case, such a license may not be available on commercially reasonable terms or at all. In addition, we may be subject to claims that we are infringing other intellectual property rights, such as trademarks or copyrights, or misappropriating the trade secrets of others, and to the extent that our employees, consultants or contractors use intellectual property or proprietary information owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

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

We license certain key intellectual property from third parties, and the loss of our license rights could have a materially adverse effect on our business.

We are a party to a number of technology licenses that are important to our business and expect to enter into additional licenses in the future. For example, we rely on an exclusive license to certain patents, proprietary technology and know-how from UC, which we believe cover brincidofovir. We also have an exclusive license to certain patents covering inventions of the UM. If we fail to comply with our obligations under our license agreements, or we are subject to a bankruptcy, the licensor may have the right to terminate the license, in which event we would not be able to develop or market products covered by the license, including in the case of the UC license, brincidofovir, which would have a materially adverse effect on our business.

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

Competitors may infringe or otherwise violate our patents, the patents of our licensors or our other intellectual property rights. To
counter infringement or unauthorized use, we may be required to file legal claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing. The initiation of a claim against a third party may also cause the third party to bring counter-claims against us.

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

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

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

Periodic maintenance fees on any issued patent are due to be paid to the U.S. PTO and foreign patent agencies in several stages over the lifetime of the patent. The U.S. PTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process.

While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. 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. If we or our licensors that control the prosecution and maintenance of our licensed patents fail to maintain the patents and patent applications covering our product candidates, we may lose our rights and our competitors might be able to enter the market, which would have a material adverse effect on our business.

Risks Related to Our United States Government Contracts and Grants

All of our immediately foreseeable future revenues to support the development of brincidofovir for the treatment of smallpox are dependent upon our contract with the Biomedical Advanced Research and Development Authority (BARDA), and if we do not receive all of the funds under the BARDA contract we anticipate that we will suspend or terminate our smallpox program.

Substantially all of our revenues that support the development of brincidofovir for the treatment of smallpox have been derived from prior government grants and our current development contract with BARDA. Our contract with BARDA is for the development of brincidofovir for the treatment of smallpox. It is divided into a base segment and four option segments. We substantially completed performance under the first option segment of the contract in August 2014 and are currently performing under the second and third option segments of the contract which are scheduled to end in August 2019 and March 2019, respectively. Subsequent option

segments are not subject to automatic renewal and are not exercisable at our discretion. There can be no assurance that we will reach agreement with BARDA on the most appropriate development pathway or that the FDA will ultimately agree with the experiments which we perform or the appropriateness of the results of these experiments for approval of brincidofovir for smallpox. In addition, there can be no assurance that any of the subsequent option segments will be exercised or that we will continue to receive revenues under this contract once the current option segments are completed. We do not anticipate continuing this program without ongoing support from BARDA.

Additionally, the contract provides for reimbursement of the costs of the development of brincidofovir for the treatment of smallpox that are allowable under the Federal Acquisition Regulation (FAR), plus the payment of a fixed fee. It does not include the manufacture of brincidofovir for the Strategic National Stockpile. There can be no assurances that this contract will continue, that BARDA will extend the contract for additional option segments, that any such extension would be on favorable terms, or that we will be able to enter into new contracts with the United States government to support our smallpox program. Changes in government budgets and agendas may result in a decreased and de-prioritized emphasis on supporting the discovery and development of brincidofovir for the treatment of smallpox. In such event, BARDA is not required to continue funding our existing contract. Any such reduction in our revenues from BARDA or any other government contract could materially adversely affect our financial condition and results of operations. In addition, if we do not receive all of the funds under the BARDA contract, we anticipate that we will suspend or terminate our program for the development of brincidofovir for the treatment of smallpox.

There can be no assurances that we will be able to enter into a contract with BARDA to act as the sole supplier for the procurement of brincidofovir for the treatment of smallpox.

In April 2015, BARDA posted a notice of intent to use other than full and open competition to award a sole source contract to us for the procurement of brincidofovir for the treatment of smallpox. In May 2015, BARDA posted an approved justification for the use of other than full and open competition for the contract. In July 2015, BARDA issued a RFP entitled “2015 Procurement of a Second Smallpox Antiviral Drug for the Strategic National Stockpile.” In August 2015, we submitted a response to the RFP and we subsequently engaged in discussions with BARDA regarding our response. The issuance of that RFP did not culminate with agreement for the sole source supply of brincidofovir for the Strategic National Stockpile.

We remain in discussions with BARDA regarding the potential to supply brincidofovir to the Strategic National Stockpile, however, there can be no assurances regarding any such procurement. We continue to receive funding under an advanced research and development contract for the development of brincidofovir for the treatment of smallpox. We are currently evaluating brincidofovir for efficacy in two different animal models to support potential approval under the FDA’s animal rule.

Through our continuing development contract with BARDA, we recently completed the in-life segment of our second rabbitpox efficacy study and initiated the pivotal efficacy study in the mouse model (ectromelia virus). We believe that efficacy data from this model could serve as the second animal model to support the approval of brincidofovir for the treatment of smallpox.

Unfavorable provisions in government contracts, including our contract with BARDA, may harm our business, financial condition and operating results.

United States government contracts typically contain unfavorable provisions and are subject to audit and modification by the government at its sole discretion, which will subject us to additional risks. For example, under our contract with BARDA, the U.S. government has the power to unilaterally:

•

audit and object to any BARDA contract-related costs and fees on grounds that they are not allowable under the FAR, and require us to reimburse all such costs and fees;

- suspend or prevent us for a set period of time from receiving new contracts or extending our existing contract based on violations or suspected violations of laws or regulations;
- claim nonexclusive, nontransferable rights to product manufactured and intellectual property developed under the BARDA contract and may, under certain circumstances, such as circumstances involving public health and safety, license such inventions to third parties without our consent;
- cancel, terminate or suspend our BARDA contract based on violations or suspected violations of laws or regulations;
- terminate our BARDA contract in whole or in part for the convenience of the government for any reason or no reason, including if funds become unavailable to the applicable governmental agency;
- reduce the scope and value of our BARDA contract;
- decline to exercise an option to continue the BARDA contract;
- direct the course of a development program in a manner not chosen by the government contractor;
- require us to perform the option segments even if doing so may cause us to forego or delay the pursuit of other opportunities with greater commercial potential;
- take actions that result in a longer development timeline than expected; and

- change certain terms and conditions in our BARDA contract.

The U.S. government also has the right to terminate the BARDA contract if termination is in the government's interest, or if we default by failing to perform in accordance with the milestones set forth in the contract. Termination-for-convenience provisions generally enable us to recover only our costs incurred or committed (plus a portion of the agreed fee) and settlement expenses on the work completed prior to termination. Except for the amount of services received by the government, termination-for-default provisions do not permit recovery of fees.

In addition, we must comply with numerous laws and regulations that affect how we conduct business with the United States government. Among the most significant government contracting regulations that affect our business are:

- FAR, and agency-specific regulations supplements to the FAR, which comprehensively regulate the procurement, formation, administration and performance of government contracts and implement federal procurement policy in numerous areas, such as employment practices, protection of the environment, accuracy and retention periods of records, recording and charging of costs, treatment of laboratory animals and human subject research;
- business ethics and public integrity obligations, which govern conflicts of interest and the hiring of former government employees, restrict the granting of gratuities and funding of lobbying activities and incorporate other requirements such as the Anti-Kickback Act and the Foreign Corrupt Practices Act;
- export and import control laws and regulations; and
- laws, regulations and executive orders restricting the use and dissemination of information classified for national security purposes and the exportation of certain products and technical data.

Furthermore, we may be required to enter into agreements and subcontracts with third parties, including suppliers, consultants and other third-party contractors, in order to satisfy our contractual obligations pursuant to our agreements with the U.S. government. Negotiating and entering into such arrangements can be time-consuming and we may not be able to reach agreement with such third parties. Any such agreement must also be compliant with the terms of our government contract. Any delay or inability to enter into such arrangements or entering into such arrangements in a manner that is non-compliant with the terms of our contract, may result in violations of our contract.

As a result of these unfavorable provisions, we must undertake significant compliance activities. The diversion of resources from commercial programs to these compliance activities, as well as the exercise by the U.S. government of any rights under these provisions, could materially harm our business.

Our business is subject to audit by the U.S. government, including under our contract with BARDA, and a negative audit could adversely affect our business.

United States government agencies, such as the DHHS, routinely audit and investigate government contractors and recipients of federal grants, including our contract with BARDA. These agencies review a contractor's performance under its contracts, cost structure and compliance with applicable laws, regulations and standards.

The DHHS can also review the adequacy of, and a contractor's compliance with, its internal control systems and policies, including the contractor's purchasing, property, estimating, compensation and management information systems. Any costs found to be improperly allocated to a specific contract will not be reimbursed, while such costs already reimbursed must be refunded. If an audit uncovers improper or illegal activities, we may be subject to civil and criminal penalties and administrative sanctions, including:

- termination of contracts;
- forfeiture of profits;
- suspension of payments;

- fines; and
- suspension or prohibition from conducting business with the U.S. government.

In addition, we could suffer serious reputational harm if allegations of impropriety were made against us by the U.S. government, which could adversely affect our business.

Agreements with government agencies may lead to claims against us under the Federal False Claims Act, and these claims could result in substantial fines and other penalties.

The biopharmaceutical industry is, and in recent years has been, under heightened scrutiny as the subject of government investigations and enforcement actions. Our BARDA contract is subject to substantial financial penalties under the Federal Civil

Monetary Penalties Act and the False Claims Act. The False Claims Act imposes liability on any person who, among other things, knowingly presents, or causes to be presented, a false record or statement material to a false or fraudulent claim paid or approved by the government. Under the False Claims Act's "whistleblower" provisions, private enforcement of fraud claims against businesses on behalf of the U.S. government has increased due in part to amendments to the False Claims Act that encourage private individuals to sue on behalf of the government. These whistleblower suits, known as qui tam actions, may be filed by private individuals, including present and former employees. The False Claims Act provides for treble damages and significant civil monetary penalties per false claim. If our operations are found to be in violation of any of these laws, or any other governmental regulations that apply to us, we may be subject to penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from the Medicare and Medicaid programs, and the curtailment or restructuring of our operations. Any penalties, damages, fines, exclusions, curtailment, or restructuring of our operations could adversely affect our ability to operate our business and our financial results.

Risks Related to Our Business Operations and Industry

Increasing demand for compassionate use of our unapproved therapies could result in losses.

We are developing brincidofovir for life-threatening illnesses for which there are currently limited to no available therapeutic options. During 2014, we were the target of an active and disruptive social media campaign related to a request for access to our unapproved drug, brincidofovir. If we experience similar social media campaigns in the future, we may experience significant disruption to our business which could result in losses.

Recent media attention to individual patients' expanded access requests has resulted in the introduction of legislation at the local and national level referred to as "Right to Try" laws, such as the Right to Try Act, which are intended to give patients access to unapproved therapies. New and emerging legislation regarding expanded access to unapproved drugs for life-threatening illnesses could negatively impact our business in the future.

A possible consequence of both activism and legislation in this area is the need for us to initiate an unanticipated expanded access program or to make brincidofovir more widely available sooner than anticipated. We are a small company with limited resources and unanticipated trials or access programs could result in diversion of resources from our primary goals.

In addition, patients who receive access to unapproved drugs through compassionate use or expanded access programs have life-threatening illnesses and have exhausted all other available therapies. The risk for serious adverse events in this patient population is high which could have a negative impact on the safety profile of brincidofovir, which could cause significant delays or an inability to successfully commercialize brincidofovir, which could materially harm our business. We may also need to restructure or pause ongoing compassionate use and/or expanded access programs in order to perform the controlled clinical trials required for regulatory approval and successful commercialization of brincidofovir, which could prompt adverse publicity or other disruptions related to current or potential participants in such programs.

If we fail to comply with the extensive legal and regulatory requirements affecting the health care industry, we could face increased costs, delays in the development of our product candidates, penalties and a loss of business.

Our activities, and the activities of our collaborators, partners and third-party providers, are subject to extensive government regulation and oversight both in the United States and in foreign jurisdictions. The FDA and comparable agencies in other jurisdictions directly regulate many of our most critical business activities, including the conduct of preclinical and clinical studies, product manufacturing, advertising and promotion, product distribution, adverse event reporting and product risk management. States increasingly have been placing greater restrictions on the marketing

practices of healthcare companies. In addition, pharmaceutical and biotechnology companies have been the target of lawsuits and investigations alleging violations of government regulations, including claims asserting submission of incorrect pricing information, impermissible off-label promotion of pharmaceutical products, payments intended to influence the referral of federal or state healthcare business, submission of false claims for government reimbursement, antitrust violations, violations of the Foreign Corrupt Practices Act, or violations related to environmental matters. Violations of governmental regulation may be punishable by criminal, civil and administrative sanctions, including fines and civil monetary penalties and exclusion from participation in government programs, including Medicare and Medicaid. In addition to penalties for violation of laws and regulations, we could be required to delay or terminate the development of our product candidates, or we could be required to repay amounts we received from government payers, or pay additional rebates and interest if we are found to have miscalculated the pricing information we have submitted to the government. Whether or not we have complied with the law, an investigation into alleged unlawful conduct could increase our expenses, damage our reputation, divert management time and attention and adversely affect our business.

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on the principal members of our executive team. While we have entered into employment agreements or offer letters with each of our executive officers, any of them could leave our employment at any time, as all of our employees are "at will" employees. To help attract, retain, and motivate qualified employees, we use share-based incentive awards such as employee stock options and restricted stock units. Due to the decline in our stock price that has occurred since December 2015, a large percentage of the options held by our employees are underwater. As of December 31, 2018, approximately 98% of all outstanding options had an exercise price above the closing price of the stock on that date. As a result, the current situation provides a considerable challenge to maintaining employee motivation, as well as creating a serious threat to retention until a recovery commences. If our share-based compensation ceases to be viewed as a valuable benefit, our ability to attract, retain, and motivate employees could be weakened, which could harm our results of operations.

We do not maintain "key person" insurance for any of our executives or other employees. Recruiting and retaining other qualified employees for our business, including scientific and technical personnel, will also be critical to our success. There is currently a shortage of appropriately skilled executives in our industry, which is likely to continue. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. As a result, competition for skilled personnel is intense and the turnover rate can be high. We may not be able to attract and retain personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. In addition, failure of any of our clinical studies may make it more challenging to recruit and retain qualified personnel. The inability to recruit or loss of the services of any executive or key employee may adversely affect the progress of our research, development and commercialization objectives.

In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us, which could also adversely affect the progress of our research, development and commercialization objectives.

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

The use of our product candidates, including brincidofovir, in clinical studies and the sale of any products for which we obtain marketing approval exposes us to the risk of product liability claims. Product liability claims might be brought against us by consumers, health care providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. On occasion, large judgments have been awarded in class action lawsuits based on drugs that had unanticipated adverse effects. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- impairment of our business reputation and significant negative media attention;
- withdrawal of participants from our clinical studies;
- significant costs to defend the related litigation and related litigation;
- distraction of management's attention from our primary business;
- substantial monetary awards to patients or other claimants;
- inability to commercialize our product candidates, including brincidofovir; and
- decreased demand for our product candidates, if approved for commercial sale.

We currently carry $15 million in product liability insurance covering our clinical trials. Our current product liability insurance coverage may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive and in the future we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If and when we obtain marketing approval for our product candidates, we intend to expand our insurance coverage to include the sale of commercial products; however, we may be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business.

Risks associated with expanding our operations to Europe could adversely affect our business.

We currently have limited operations in Europe and plan to expand the scope of development activities taking place there. We have limited experience with conducting activities outside of the United States. International operations and business expansion plans are subject to numerous additional risks, including:

- multiple, conflicting and changing laws and regulations such as tax laws, privacy regulations, export and import restrictions, employment, immigration and labor laws, regulatory requirements, and other governmental approvals, permits and licenses;
- difficulties in staffing and managing foreign operations;
- risks associated with obtaining and maintaining, or the failure to obtain or maintain, regulatory approvals for the sale or use of our products in various countries;
- complexities associated with managing government payer systems, multiple payer-reimbursement regimes or patient self-pay systems and price controls;
- financial risks, such as longer payment cycles, difficulty enforcing contracts and collecting accounts receivable and exposure to foreign currency exchange rate fluctuations;
- general political and economic conditions in the countries we operate in, including terrorism and political unrest, curtailment of trade and other business restrictions;
- regulatory and compliance risks that relate to maintaining accurate information and control over activities that may fall within the purview of the U.S. Foreign Corrupt Practices Act, its books and records provisions or its anti-bribery provisions, or similar anti-bribery or anti-corruption laws and regulations.

Any of these risks, if encountered, could significantly increase our costs of operating internationally, prevent us from operating in certain jurisdictions, or otherwise significantly harm our future international expansion and operations, which could have a material adverse effect on our business, financial condition and results of operations.

Risks Related To Our Common Stock

The market price of our common stock is likely to be volatile, and you may not be able to resell your shares at or above your purchase price.

Prior to our initial public offering (IPO) in 2013, there was no public market for our common stock. The trading price of our common stock has been volatile, and is likely to continue to be volatile for the foreseeable future. Our stock price is subject to wide fluctuations in response to a variety of factors, including the following:

- results of clinical trials of our product candidates or those of our competitors;
- any delay in filing an application for any of our product candidates and any adverse development or perceived adverse development with respect to regulatory review of that application;
- failure to successfully develop and commercialize our product candidates, including brincidofovir;
- termination of any of our license or collaboration agreements;
- any agency or judicial enforcement actions against us;
- inability to obtain additional funding;
- regulatory or legal developments in the United States and other countries applicable to our product candidates;
- adverse regulatory decisions;
- changes in the structure of healthcare payment systems;
- inability to obtain adequate product supply for our product candidates, or the inability to do so at acceptable prices;
- introduction of new products, services or technologies by our competitors;
- failure to meet or exceed financial projections we provide to the public;

- failure to meet or exceed the estimates and projections of the investment community;
- changes in the market valuations of similar companies;
- market conditions in the pharmaceutical and biotechnology sectors, and the issuance of new or changed securities analysts' reports or recommendations;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors;
- significant lawsuits (including patent or stockholder litigation), and disputes or other developments relating to proprietary rights (including patents, litigation matters and our ability to obtain patent protection for our technologies);
- additions or departures of key scientific or management personnel;
- sales of our common stock by us or our stockholders in the future;
- trading volume of our common stock;
- general economic, industry and market conditions; and

- the other factors described in this “Risk Factors” section.

In addition, the stock market in general, and The Nasdaq Global Market in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance.

The resignation of our former Chief Executive Officer may be disruptive and our ability to successfully manage this transition could impact our business.

On February 6, 2019, we announced that M. Michelle Berrey had resigned as our President and Chief Executive Officer, and that our Board of Directors created a new position to be known as the Office of the Chief Executive Officer, and appointed W. Garrett Nichols, Timothy W. Trost and Michael A. Alrutz as the members of the Office of the Chief Executive Officer. Leadership transitions can be difficult to manage and may cause disruptions to our operations. The leadership transition may also increase the likelihood of turnover among our employees and result in changes in our business strategy, which may create uncertainty and negatively impact our ability to execute our business strategy quickly and effectively. The Chief Executive Officer transition may also impact our relationships with customers and suppliers, and create uncertainty among investors, employees, creditors and others concerning our future direction and performance. Any significant disruption, uncertainty or change in business strategy could adversely affect our business, financial condition and operating results.

Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

Based upon shares of common stock outstanding as of December 31, 2018, our then executive officers, directors, 5% stockholders (known to us through available information) and their affiliates beneficially owned approximately 38% of our voting stock. Therefore, these stockholders have the ability to substantially influence us through this ownership position. For example, these stockholders, if they choose to act together, may be able to influence the election of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This concentration of voting power could delay or prevent an acquisition of our company on terms that other stockholders may desire.

Failure to establish and maintain adequate finance infrastructure and accounting systems and controls could impair our ability to comply with the financial reporting and internal controls requirements for publicly traded companies.

As a public company, we operate in an increasingly demanding regulatory environment, which requires us to comply with the Sarbanes-Oxley Act of 2002, and the related rules and regulations of the Securities and Exchange Commission, expanded disclosure requirements, accelerated reporting requirements and more complex accounting rules. Company responsibilities required by the Sarbanes-Oxley Act include establishing and maintaining corporate oversight and adequate internal control over financial reporting and disclosure controls and procedures. Effective internal controls are necessary for us to produce reliable financial reports and are important to help prevent financial fraud.

Our compliance with Section 404 of the Sarbanes-Oxley Act has required and will continue to require that we incur substantial accounting expense and expend significant management efforts. In this or future years, our testing, or the subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls that we would be required to remediate in a timely manner so as to be able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act each year. If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act in a timely manner each year, we could be subject to sanctions or investigations by the

Securities and Exchange Commission, The Nasdaq Stock Market or other regulatory authorities which would require additional financial and management resources and could adversely affect the market price of our common stock. Furthermore, if we cannot provide reliable financial reports or prevent fraud, our business and results of operations could be harmed and investors could lose confidence in our reported financial information.

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

We expect that significant additional capital will be needed in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. Such sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders.

Pursuant to our 2013 Equity Incentive Plan (the 2013 Plan), our management is authorized to grant stock options to our employees, directors and consultants. The number of shares available for future grant under our 2013 Plan will automatically increase on January 1st each year, through January 1, 2023, by an amount equal to 4.0% of all shares of our capital stock outstanding as of December 31st of the preceding calendar year, subject to the ability of our board of directors to take action to reduce the size of such increase in any given year. In addition, our board of directors may grant or provide for the grant of rights to purchase shares of our common stock pursuant to the terms of our 2013 Employee Stock Purchase Plan (ESPP). The number of shares of our common stock reserved for issuance under our ESPP will automatically increase on January 1st each year, through January 1, 2023, by an amount equal to the lesser of 422,535 shares or one percent of all shares of our capital stock outstanding as of December 31st of the preceding calendar year, subject to the ability of our board of directors to take action to reduce the size of such increase in any given year. Unless our board of directors elects not to increase the number of shares underlying our 2013 Plan and ESPP each year, our stockholders may experience additional dilution, which could cause our stock price to fall.

We have broad discretion in the use of the net proceeds from our financing transactions and may not use them effectively.

Our management has broad discretion in the application of the net proceeds from our financing transactions. Because of the number and variability of factors that will determine our use of the net proceeds from our financing transactions, their ultimate use may vary substantially from their currently intended use. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our product candidates. Pending their use, we have invested the net proceeds from our financing transactions in short-term, investment-grade, interest-bearing securities. These investments may not yield a favorable return to our stockholders.

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

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because pharmaceutical companies have experienced significant stock price volatility in recent years, and also because our stock price decreased significantly following announcement of results from our Phase 3 SUPPRESS trial. If we face such litigation, it could result in substantial costs and a diversion of management’s attention and resources, which could harm our business.

Comprehensive tax reform could adversely affect our business and financial condition.

On December 22, 2017, President Trump signed into law the Tax Act which significantly revises the Internal Revenue Code of 1986, as amended. The Tax Act, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits. Notwithstanding the reduction in the corporate income tax rate, the overall impact of the Tax Act is uncertain and our business and financial condition could be adversely affected. In addition, it is uncertain if and to what extent various states will conform to the Tax Act. The impact of this tax reform on holders of our common stock is also uncertain and could be adverse. We urge our stockholders to consult with their legal and tax advisors with respect to this legislation and the potential tax consequences of investing in or holding our common stock.

Our effective tax rate may fluctuate, and we may incur obligations in tax jurisdictions in excess of accrued amounts.

Our effective tax rate is derived from a combination of applicable tax rates in the various places that we operate. In preparing our financial statements, we estimate the amount of tax that will become payable in each of such places. Nevertheless, our effective tax rate may be different than experienced in the past due to numerous factors, including passage of the Tax Act, the results of examinations and audits of our tax filings, our inability to secure or sustain acceptable agreements with tax authorities, changes in accounting for income taxes and changes in tax laws. Any of these factors could cause us to experience an effective tax rate significantly different from previous periods or our current expectations and may result in tax obligations in excess of amounts accrued in our financial statements.

Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.

Our U.S. net operating loss, or NOL, carryforwards generated in tax years ending on or prior to December 31, 2017, are only permitted to be carried forward for 20 years under applicable U.S. tax law. Under the Tax Act, our federal NOLs generated in tax years ending after December 31, 2017, may be carried forward indefinitely, but the deductibility of such federal NOLs

generated in tax years beginning after December 31, 2017, is limited. It is uncertain if and to what extent various states will conform to the Tax Act. In addition, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, 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 NOL carryforwards and other pre-change U.S. tax attributes (such as research tax credits) to offset its post-change income or taxes may be limited. We have determined that a Section 382 ownership change occurred in 2002 and 2007 resulting in limitations of at least $64,000 and $762,000, respectively, of losses incurred prior to the respective ownership change dates. In addition, we have determined that another Section 382 ownership change occurred in 2013 with our IPO, our most recent private placement and other transactions that have occurred since 2007, resulting in a limitation of at least $6.7 million of losses incurred prior to the ownership change date. We may also experience ownership changes in the future as a result of subsequent shifts in our stock ownership. As a result, our pre-2018 NOL carryforwards may expire prior to being used, and our NOL carryforwards generated in 2018 and thereafter will be subject to a percentage limitation. In addition, it is possible that we have in the past undergone, and in the future may undergo, additional ownership changes that could limit our ability to use all of our pre-change NOLs and other pre-change tax attributes (such as research tax credits) to offset our post-change income or taxes. Similar provisions of state tax law may also apply to limit our use of accumulated state tax attributes. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. As a result, we may be unable to use all or a material portion of our NOLs and other tax attributes.

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

We have never declared or paid any cash dividends on our common stock. We currently anticipate that we will retain any future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. As a result, capital appreciation, if any, of our common stock would be your sole source of gain on an investment in our common stock for the foreseeable future.

Provisions in our corporate charter documents and under Delaware law could make it more difficult for a third party to acquire us or increase the cost of acquiring us, even if doing so would benefit our stockholders and may prevent attempts by our stockholders to replace or remove our current management.

Some provisions of our charter documents and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders and may prevent attempts by our stockholders to replace or remove our current management. These provisions include:

- authorizing the issuance of "blank check" preferred stock, the terms of which may be established and shares of which may be issued without stockholder approval which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors;
- allowing the authorized number of our directors to be changed only by resolution of our board of directors;
- limiting the removal of directors;
- creating a staggered board of directors;
- requiring that stockholder actions must be effected at a duly called stockholder meeting and prohibiting stockholder actions by written consent;
- eliminating the ability of stockholders to call a special meeting of stockholders; and
- establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at duly called stockholder meetings.

The amendment of any of these provisions, with the exception of the ability of our board of directors to issue shares of preferred stock and designate any rights, preferences and privileges thereto, would require the affirmative vote of the holders of at least 66 2/3 percent of the voting power of all of our then outstanding common stock.

These provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management. In addition, we are subject to Section 203 of the Delaware General Corporation Law, which generally prohibits a Delaware corporation from engaging in any of a broad range of business combinations with an interested stockholder for a period of three years following the date on which the stockholder became an interested stockholder, unless such transactions are approved by our board of directors. This provision could have the effect of delaying or preventing a change of control, whether or not it is desired by or beneficial to our stockholders. Further, other provisions of Delaware law may also discourage, delay or prevent someone from acquiring us or merging with us.

Risks Related to Information Technology

Significant disruptions of information technology systems or breaches of data security could adversely affect our business.

Our business is increasingly dependent on critical, complex, and interdependent information technology (IT) systems, including Internet-based systems, to support business processes as well as internal and external communications. The size and complexity of our IT systems make us potentially vulnerable to IT system breakdowns, malicious intrusion, and computer viruses, which may result in the impairment of our ability to operate our business effectively.

In addition, our systems are potentially vulnerable to data security breaches-whether by employees or others-which may expose sensitive data to unauthorized persons. Such data security breaches could lead to the loss of trade secrets or other intellectual property, or could lead to the public exposure of personal information (including sensitive personal information) of our employees, clinical trial patients, customers, business partners and others.

Any such disruption or security breach could result in legal proceedings, liability under laws that protect the privacy of personal information, regulatory penalties, disruptions to our operations and collaborations, and damage to our reputation, which could harm our business and results of operations.

Increasing use of social media could give rise to liability, breaches of data security, or reputational damage.

We and our employees are increasingly utilizing social media tools as a means of communication both internally and externally. Despite our efforts to monitor evolving social media communication guidelines and comply with applicable rules, there is risk that the use of social media by us or our employees to communicate about our products or business may cause us to be found in violation of applicable laws and regulations. In addition, our employees may knowingly or inadvertently make use of social media in ways that may not comply with our social media policy or other legal or contractual requirements, which may give rise to liability, lead to the loss of trade secrets or other intellectual property, or result in public exposure of personal information of our employees, clinical trial patients, customers, and others. Furthermore, negative posts or comments about us or our products in social media could seriously damage our reputation, brand image, and goodwill.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

Our corporate headquarters are located at 2505 Meridian Parkway, Suite 100, Durham, North Carolina 27713 in a facility we lease encompassing approximately 24,862 square feet of office space. The leases for this facility expire in February 2021.We separately lease laboratory space in Durham and Research Triangle Park, North Carolina, encompassing a total of approximately 10,274 square feet. The leases for this laboratory space in Durham and Research Triangle Park expire in July 2021 and August 2021, respectively.

We believe that our property and equipment are generally well maintained and in good operating condition.

ITEM 3. LEGAL PROCEEDINGS

None.

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 began trading on The Nasdaq Global Market on April 11, 2013 under the symbol "CMRX." Prior to such time, there was no public market for our common stock. The following table sets forth the high and low sales prices per share of our common stock as reported on The Nasdaq Global Market for the periods indicated. Such quotations represent inter-dealer prices without retail markup, markdown or commission and may not necessarily represent actual transactions.

	Year Ended December 31, 2018	
	High	Low
First Quarter	$5.94	$4.58
Second Quarter	$5.22	$4.35
Third Quarter	$5.04	$3.57
Fourth Quarter	$4.00	$2.08

	Year Ended December 31, 2017	
	High	Low
First Quarter	$6.64	$4.33
Second Quarter	$6.57	$4.28
Third Quarter	$5.60	$4.30
Fourth Quarter	$5.54	$4.17

Stock Performance Graph[(1)]

The following graph shows a comparison from December 31, 2013 through December 31, 2018 of the cumulative total return for our common stock, the Nasdaq Biotechnology Index (NBI) and the Nasdaq Composite Index (CCMP). The graph assumes as initial investment of $100 on December 31, 2013. The comparisons in the graph below are based upon historical data and are not intended to forecast or be indicative of possible future performance of our common stock or Indexes.

Comparison of Cumulative Total Return*
Among Chimerix, Inc., the Nasdaq Biotechnology Index and the Nasdaq Composite Index

(1) This section is not "soliciting material," is not deemed "filed" with the SEC and is not to be incorporated by reference in any of our filings under the Securities Act or the Exchange Act whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.

* Assuming the investment of $100 on 12/31/2013 (and the reinvestment of dividends thereafter) in each of (i) Chimerix, Inc.'s common stock, (ii) the Nasdaq Biotechnology Index and (iii) the Nasdaq Composite Index.

Stockholders

As of February 26, 2019, there were 33 stockholders of record of our common stock, which excludes stockholders whose shares were held in nominee or street name by brokers. The actual number of common stockholders is greater than the number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividend Policy

We have never declared or paid any cash dividends on our common stock. We currently intend to retain all available funds and any future earnings to support our operations and finance the growth and development of our business. We do not intend to pay cash dividends on our common stock for the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our board of directors and will depend upon, among other factors, our results of operations, financial condition, capital requirements, contractual restrictions, business prospects and other factors our board of directors may deem relevant.

Recent Sales of Unregistered Securities

None.

Securities Authorized for Issuance Under Equity Compensation Plans

Information about our equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

We did not purchase any of our securities during the period covered by this Annual Report.

ITEM 6. SELECTED FINANCIAL DATA

The following selected consolidated financial data should be read together with our consolidated financial statements and related notes and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” appearing elsewhere in this Annual Report. The selected financial data in this section are not intended to replace our consolidated financial statements and the related notes. Our historical results are not necessarily indicative of the results that may be expected in the future.

We derived the following selected Consolidated Statement of Operations and Comprehensive Loss Data for the years ended December 31, 2018, 2017, and 2016 and the selected Consolidated Balance Sheet Data as of December 31, 2018 and 2017 from our audited consolidated financial statements and related notes appearing elsewhere in this Annual Report (in thousands, except share and per share data).

Consolidated Statement of Operations and Comprehensive Loss Data	Years Ended December 31, 2018	2017	2016	2015	2014
Revenues:					
Contract revenue	$7,216	$4,494	$5,702	$9,214	$4,040
Collaboration and licensing revenue	—	—	—	1,548	—
Total revenues	7,216	4,494	5,702	10,762	4,040
Operating expenses:					
Research and development	55,239	49,448	58,647	97,717	45,379
General and administrative	23,582	27,148	25,007	31,296	17,527
Total operating expenses	78,821	76,596	83,654	129,013	62,906
Loss from operations	(71,605)	(72,102)	(77,952)	(118,251)	(58,866)
Other (expense) income:					
Unrealized loss on equity investment	(348)	(1,160)	—	—	—
Interest income (expense) and other, net	2,479	2,278	1,562	879	(446)
Net loss	$(69,474)	$(70,984)	$(76,390)	$(117,372)	$(59,312)
Net loss per share, basic and diluted	$(1.43)	$(1.51)	$(1.65)	$(2.67)	$(1.80)
Weighted-average shares outstanding, basic and diluted	48,593,435	46,963,430	46,267,064	43,878,326	33,003,714

Consolidated Balance Sheet Data	Years Ended December 31, 2018	2017	2016	2015	2014
Cash and cash equivalents	$81,106	$18,548	$51,463	$20,605	$128,462
Short-term investments, available-for-sale (1)	105,424	132,972	180,558	199,729	106,114
Working capital	176,492	143,337	226,360	208,658	220,390
Long-term investments (1)	—	76,731	47,407	124,040	52,973
Total assets	190,714	235,230	286,770	355,992	291,878
Loan payable, net, current portion (2)	—	—	—	—	4,296
Accumulated deficit	(556,262)	(486,788)	(415,804)	(339,414)	(222,042)
Total stockholders' equity (deficit)	$177,604	$221,810	$276,224	$335,459	$274,636

(1) Further details of investments is available in "Notes to Consolidated Financial Statements, Note 1. Fair Value of Financial Instruments" in Item 8 of this Annual Report.

(2) Loan payable is net of debt discount.

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The following discussion and analysis should be read in conjunction with "Selected Financial Data" and our financial statements and related notes included elsewhere in this Annual Report. This discussion and analysis and other parts of this Annual Report contain forward-looking statements based upon current beliefs, plans and expectations that involve risks, uncertainties and assumptions, such as statements regarding our plans, objectives, expectations, intentions and projections. Our actual results and the timing of selected events could differ materially from those anticipated in these forward-looking statements as a result of several factors, including those set forth under "Risk Factors" and elsewhere in this Annual Report. You should carefully read the "Risk Factors" section of this Annual Report to gain an understanding of the important factors that could cause actual results to differ materially from our forward-looking statements. Please also see the section entitled "Forward-Looking Statements."

Overview

Chimerix, Inc. is a biotechnology company committed to discovering, developing and commercializing medicines that address significant, unmet medical needs. We were founded in 2000 based on the promise of our proprietary lipid conjugate technology to unlock the potential of some of the most broad-spectrum antivirals by enhancing their antiviral activity and safety profiles in

convenient dosing regimens. Our lead compound, brincidofovir (BCV), is in development as an oral and intravenous (IV) formulation for the prevention and treatment of DNA viruses, including smallpox, adenoviruses, and the human herpesviruses.

Recent Developments

AdAPT Study of Oral Brincidofovir

The AdAPT study (Adenovirus after Allogeneic Pediatric Transplantation) is open for enrollment at sites in the United States, the United Kingdom, and in continental Europe. All currently targeted countries and clinical sites are planned to be open for enrollment by the end of the first quarter of 2019, however additional sites may be added. This study is targeting enrollment of 141 pediatric allogeneic HCT recipients with confirmed AdV infection. Patients are randomized 2:1 to receive short-course oral BCV or local standard-of-care (SOC) treatment at approximately 40 sites in Europe and the United States.

The primary endpoint of the study is a comparison of AdV viral burden (as measured by AdV DNA levels in blood) over 16 weeks in subjects treated with short-course oral BCV versus those who receive local SOC. The study is 90% powered to show the superiority of reduced adenoviral burden in BCV-treated patients compared to SOC. The study is also designed to evaluate the correlation of adenoviral burden (and its clearance) with clinical outcomes, including survival. A strong correlation between AdV viral burden and mortality was described in data collected from the AdVance study. In the AdVance study, patients with the highest average AdV viral burden over 16 weeks had the highest observed mortality. In addition, across the pediatric patients with AdV viremia, each 1.0 $\log_{10}$ increase in average AdV burden over 16 weeks was associated with a two-fold increase in mortality. We have faced regulatory and site initiation delays in the implementation of this study. In addition, we have observed lower than anticipated incidence at the centers that have been initiated to date. Based on a thorough re-evaluation of current screening and enrollment rates, we now project that enrollment in AdAPT will be substantially delayed beyond 2019. While some recently initiated sites are historically more active in transplantation, we continue to evaluate strategies to accelerate the time to completion of the study, including opening further AdAPT sites, and possibly re-considering the targeted number of patients for full enrollment. The Company plans to provide an update on AdAPT enrollment in mid-2019.

In February 2019 we submitted a Type C meeting request with the FDA to review the AdVance data and virologic endpoints. We believe this data will help support the virologic endpoint from our ongoing AdAPT clinical trial.

Oral Treatment for Smallpox

We are collaborating with the Biomedical Advanced Research and Development Authority (BARDA) for the development of BCV as a potential medical countermeasure for smallpox. Efficacy is to be demonstrated via two animal models under the FDA's Animal Efficacy Rule. This rule allows for testing of investigational drugs in animal models to support the effectiveness of the drug in diseases in which human clinical studies are not ethical or feasible. In January 2019, we received positive preliminary top-line results of the in-life part of our adjunct rabbit smallpox study that was conducted under the Animal Efficacy Rule. The study was designed to determine the effect of administering BCV to animals at certain times (3, 4, 5 or 6 days) after inoculation with the rabbitpox virus. These preliminary results are subject to further audit, however, based on these findings the study met its primary endpoint. The topline survival results are as follows:

BCV treatment 3 days post-infection	BCV treatment 4 days post-infection	BCV treatment 5 days post-infection	BCV treatment 6 days post-infection	No treatment (placebo)
29/29 (100%)	26/29 (90%)	20/29 (69%)	20/29 (69%)	

Overall Survival					8/28 (29%)
P-value vs. Group 5	<0.0001	<0.0001	0.0014	0.0014	0

The differences in survival rate observed between each group of animals that received BCV and the animals that did not are statistically significant. Data from this study are in-line with those reported in 2015 from our first pivotal study in the rabbitpox model.

In February 2019, we initiated a pivotal study in the mouse ectromelia model, which constitutes our second animal model as described in the Animal Efficacy Rule. We anticipate data from this study in the second half of 2019 and, contingent upon the results of the animal efficacy studies, we plan to submit marketing applications in 2020.

IV Brincidofovir Progresses to Phase 2 Studies

We are continuing to open sites in the United States and Europe for enrollment in our IV BCV Phase 2 studies in adult allogeneic HCT recipients with AdV. These studies may provide data on other viral infections such as CMV and/or BKV in patients with multi-viral infections. These studies are the first-in-patient studies to demonstrate the safety and tolerability and pharmacokinetic profile of multiple doses of IV BCV in adult HCT recipients. We will also evaluate the relationship between dose and change from baseline in AdV in blood and stool. Data from these studies are expected to inform the design of future Phase 2/3 studies. Similar to AdAPT, we have faced regulatory and site initiation delays in the implementation of these studies. We have also observed lower than anticipated incidence at the study 210/211 centers that have been initiated, which has caused enrollment to occur more slowly than expected. We plan to provide a study update in mid-2019.

Data from these studies will inform the dose and dosing regimen for our potential Multi Viral Protection (MVP)-Peds study and potential studies of IV BCV for other DNA viruses, such as BKV or HHV-6.

The improved drug concentrations in the central nervous system (CNS) achieved with IV brincidofovir in animals could support the study of IV brincidofovir in viral CNS infections such as herpes encephalitis, HHV-6 encephalitis, JC virus infection.

CMX521 for Norovirus

CMX521 is a nucleoside analog identified from our proprietary Chemical Library which targets the norovirus polymerase, a part of the virus that is common to all strains and is required for viral replication. It therefore has the potential to be active against the multiple genetically diverse norovirus strains that circulate each year and cause disease in humans.

We previously presented the safety and tolerability data from a Phase 1 study of CMX521, which supported continued development of the first small molecule in clinical development for prophylaxis or treatment of norovirus. Evaluation of active antiviral concentrations in gastrointestinal biopsies indicate that improved intracellular delivery is needed prior to conducting efficacy studies. The norovirus research and development program has been paused indefinitely.

Brincidofovir Expanded Access Program

We continue to receive requests for BCV via our expanded access and named patient programs. During 2018, we granted almost 340 requests for brincidofovir for the treatment of AdV, highlighting the continued unmet need in this area.

Financial Overview

Revenues

To date, we have not generated any revenue from product sales. All of our revenue to date has been derived from a government grant and contract and the receipt of up-front proceeds under our collaboration and license agreements.

In February 2011, we entered into a contract with BARDA, a U.S. governmental agency that supports the advanced research and development, manufacturing, acquisition, and stockpiling of medical countermeasures. The contract originally consisted of an initial performance period, referred to as the base performance segment, which ended on May 31, 2013, plus up to four extension periods, referred to as option segments. Subsequent option segments to the contract are not subject to automatic renewal and are not exercisable at Chimerix’s discretion. The contract is a cost

plus fixed fee development contract. Under the contract as currently in effect, we may receive up to $75.8 million in expense reimbursement and $5.3 million in fees if all remaining option segments are exercised. We are currently performing under the second and third option segments of the contract during which we may receive up to a total of $23.9 million and $14.1 million in expense reimbursement and fees, respectively. The second option segment is scheduled to end on August 1, 2019 and the third option segments is scheduled to end on March 30, 2019. Of the $75.8 million expense reimbursement and $5.3 million in fees that we may receive, approximately $74.3 million in expense reimbursement and fees has been funded. As of December 31, 2018, of the total funding the Company had invoiced an aggregate of $62.6 million with respect to the base performance segment and the first three option segments.

On December 17, 2014, we entered into a collaboration and licensing agreement with ContraVir Pharmaceuticals (Nasdaq: CTRV). In exchange for the license to CMX157 rights, we received an upfront payment consisting of 120,000 shares of ContraVir Series B Convertible Preferred Stock with a stated value of $1.2 million. In addition, we are eligible to receive clinical, regulatory and initial commercial milestones in the United States and Europe, as well as royalties and additional milestones based on commercial sales in those territories. We recognized the upfront license fee payment from ContraVir as deferred revenue for the year ended December 31, 2014, and during the second quarter of 2015 we completed our performance obligations and recorded $1.5 million

in revenue. In September 2016, we converted our shares of ContraVir Series B Convertible Preferred Stock into shares of ContraVir common stock.

In the future, we may generate revenue from a combination of product sales, license fees, milestone payments and royalties from the sales of products developed under licenses of our intellectual property. We expect that any revenue we generate will fluctuate from quarter to quarter as a result of the timing and amount of license fees, milestone and other payments, and the amount and timing of payments that we receive upon the sale of our products, to the extent any are successfully commercialized. If we fail to complete the development of our product candidates in a timely manner or obtain regulatory approval for them, our ability to generate future revenue, and our results of operations and financial position, would be materially adversely affected.

Research and Development Expenses

Since our inception, we have focused our resources on our research and development activities, including conducting preclinical studies and clinical trials, manufacturing development efforts and activities related to regulatory filings for our product candidates. We recognize research and development expenses as they are incurred. Costs for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors. We cannot determine with certainty the duration and completion costs of the current or future clinical studies of our product candidates. Our research and development expenses consist primarily of:

- fees paid to consultants and contract research organizations (CROs), including in connection with our preclinical and clinical trials, and other related clinical trial fees, such as for investigator grants, patient screening, laboratory work, clinical trial database management, clinical trial material management and statistical compilation and analysis;
- salaries and related overhead expenses, which include stock option, restricted stock unit (RSU) and employee stock purchase program compensation and benefits, for personnel in research and development functions;
- payments to third-party manufacturers, which produce, test and package our drug substance and drug product (including continued testing of process validation and stability);
- costs related to legal and compliance with regulatory requirements; and
- license fees for and milestone payments related to licensed products and technologies.

From our inception through December 31, 2018, we have incurred approximately $460.1 million in research and development expenses, of which $411.6 million relates to our development of brincidofovir. These costs were largely related to the conduct of our clinical trials of brincidofovir.

The table below summarizes our research and development expenses for the periods indicated (in thousands). Our direct research and development expenses consist primarily of external costs, such as fees paid to investigators, consultants, central laboratories and CROs, in connection with our clinical trials, preclinical development, and payments to third-party manufacturers of drug substance and drug product. We typically use our employee and infrastructure resources across multiple research and development programs.

	Years Ended December 31,		
	2018	2017	2016
Direct research and development expenses	$31,325	$24,734	$31,415
Research and development personnel costs - excluding stock-based compensation	13,488	13,490	15,035
Research and development personnel costs - stock-based compensation	5,343	7,047	7,137
Indirect research and development expenses	5,083	4,177	5,060
Total research and development expenses	$55,239	$49,448	$58,647

The successful development of our clinical and preclinical product candidates is highly uncertain. At this time, we cannot reasonably estimate the nature, timing or costs of the efforts that will be necessary to complete the remainder of the development of any of our clinical or preclinical product candidates or the period, if any, in which material net cash inflows from these product candidates may commence. This is due to the numerous risks and uncertainties associated with the development of our product candidates, including:

- the uncertainty of the scope, rate of progress and expense of our ongoing, as well as any additional, clinical trials and other research and development activities;
- the potential benefits of our candidates over other therapies;
- the ability to market, commercialize and achieve market acceptance for any of our product candidates that we are developing or may develop in the future;

- the results of ongoing or future clinical trials;
- the timing and receipt of any regulatory approvals; and
- the filing, prosecuting, defending and enforcing of patent claims and other intellectual property rights, and the expense of doing so.

A change in the outcome of any of these variables with respect to the development of a product candidate could mean a significant change in the costs and timing associated with the development of that product candidate. For example, if the FDA or another regulatory authority were to require us to conduct clinical trials beyond those that we currently anticipate will be required for the completion of clinical development of a product candidate in the United States or in Europe, or if we experience significant delays in enrollment in any of our clinical trials, we could be required to expend significant additional financial resources and time with respect to the development of that product candidate.

Brincidofovir

The majority of our research and development resources has been focused on completing our Phase 3 trial of brincidofovir for prevention of CMV in HCT recipients (SUPPRESS), our trial of brincidofovir as a treatment for AdV (AdVise), the AdAPT study in pediatric HCT recipients and our other clinical and preclinical studies and other work needed to provide sufficient data supporting the safety, tolerability and efficacy of brincidofovir for approval in the United States and equivalent health authority approval outside the United States.

In addition, pursuant to our contract with BARDA, we are evaluating brincidofovir for the treatment of smallpox. During the base performance segment of the contract, we incurred significant expense in connection with the development of orthopoxvirus animal models, the demonstration of efficacy and pharmacokinetics of brincidofovir in the animal models, the conduct of an open label clinical safety study for subjects with DNA viral infections, and the manufacture and process validation of bulk drug substance and brincidofovir 100 mg tablets. During the first option segment of the contract, we performed additional animal testing of brincidofovir. In September 2014, we initiated performance under the second option segment of the contract with BARDA and are performing additional animal testing of brincidofovir. In September 2015, we initiated performance under the third option segment which focuses on brincidofovir chemistry, manufacturing and controls at large scale.

As we progressed the development of brincidofovir, research and development expenses increased in the full-year 2018 compared to the full-year 2017. In 2019, we expect research and development expenses to remain consistent compared to 2018.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and related costs for employees in executive, finance, marketing, investor relations, information technology, legal, human resources and administrative support functions, including share-based compensation expenses and benefits. Other significant general and administrative expenses include the pre-launch activities for brincidofovir, accounting and legal services, cost of various consultants, director and officer liability insurance, occupancy costs and information systems.

We currently anticipate that our general and administrative expenses for the full-year 2019 will remain consistent compared to the full-year 2018.

Unrealized Loss on Equity Investment

Unrealized loss on equity investment consists of the decrease in fair value of our investment in ContraVir common stock for the year ended December 31, 2018. For the year ended December 31, 2017, unrealized loss on equity

investment consists of the write-down in value of our investment in ContraVir common stock which was determined to be other-than-temporarily impaired.

Interest Income and Other, Net

Interest income and other, net consists of interest earned on our cash, cash equivalents, short-term investments and long-term investments and realized gains and losses on debt investments.

Share-based Compensation

The Financial Accounting Standards Board (FASB) authoritative guidance requires that share-based payment transactions with employees be recognized in the financial statements based on their fair value and recognized as compensation expense over the vesting period. Total consolidated share-based compensation expense of $13.1 million, $16.1 million and $16.2 million was

recognized in the years ended December 31, 2018, 2017 and 2016, respectively. The share-based compensation expense recognized included expense for stock options, RSUs and our employee stock purchase plan purchase rights.

We estimate the fair value of our share-based awards to employees and directors using the Black-Scholes pricing model. This estimate is affected by our stock price as well as assumptions including the expected volatility, expected term, risk-free interest rate, expected dividend yield, expected rate of forfeiture and the fair value of the underlying common stock on the date of grant.

For performance-based RSUs, we begin to recognize the expense when it is deemed probable that the performance-based goal will be met. We evaluate the probability of achieving performance-based goals on a quarterly basis.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of financial condition and results of operations is based on our audited consolidated financial statements, which have been prepared in accordance with generally accepted accounting principles in the United States of America (GAAP). The preparation of these consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses. On an ongoing basis, we evaluate these estimates and judgments. We base our estimates on historical experience and on various assumptions that we believe to be reasonable under the circumstances. These estimates and assumptions form the basis for making judgments about the carrying values of assets and liabilities and the recording of revenues and expenses that are not readily apparent from other sources. Actual results and experiences may differ materially from these estimates. In addition, our reported financial condition and results of operations could vary if new accounting standards are enacted that are applicable to our business.

Our significant accounting policies are described in Note 1 to our audited consolidated financial statements for the year ended December 31, 2018 included in this Annual Report. We believe that our accounting policies relating to revenue recognition, research and development prepaids and accruals, investments and share-based compensation are the most critical to understanding and evaluating our reported financial results. We have identified these policies as critical because they both are important to the presentation of our financial condition and results of operations and require us to make judgments and estimates on matters that are inherently uncertain and may change in future periods. For more information regarding these policies, you should refer to Note 1 to our audited consolidated financial statements included in this Annual Report.

Revenue Recognition

The Company's revenues generally consist of (i) contract revenue - revenue generated under federal contracts, and (ii) collaboration and licensing revenue - revenue related to non-refundable upfront fees, royalties and milestone payments earned under license agreements. Revenue is recognized in accordance with the criteria outlined in Accounting Standards Codification (ASC) 606 issued by the Financial Accounting Standards Board (FASB). Following this accounting pronouncement, a five-step approach is applied for recognizing revenue, including (1) identify the contract with a customer; (2) identify the performance obligations in the contract; (3) determine the transaction price; (4) allocate the transaction price to the performance obligations in the contract; and (5) recognize revenue when, or as, the entity satisfies a performance obligation.

Biomedical Advanced Research and Development Authority (BARDA)

In February 2011, the Company entered into a contract with BARDA for the advanced development of brincidofovir as a medical countermeasure in the event of a smallpox release. Under the contract, the Company may receive up to

$75.8 million in expense reimbursement and $5.3 million in fees over the performance of 1 base segment and 4 option segments. Exercise of each option segment is solely at the discretion of BARDA. Currently, option segments 1 through 3 have been exercised. The Company assessed the services in accordance with the authoritative guidance and concluded that there is a potential of 5 separate contracts (1 base segment and four option segments) within this agreement, each of which has a single performance obligation. The transaction price for each segment, based on the transaction price as defined in each segment contract, is allocated to the single performance obligation for each contract. The transaction price is recognized over time by measuring the progress toward complete satisfaction of the performance obligation. The progress toward complete satisfaction is estimated based on the costs incurred to date relative to the total estimated costs per the terms of each contract. The Company typically invoices BARDA monthly as costs are incurred.

From our inception through December 31, 2018, we have not generated any revenue from product sales. For the same period, we have generated $100.9 million in grant and contract revenue. We recognize revenue under government grants and contracts as qualifying research activities are conducted based on invoices received from company vendors. Any amounts received in advance of performance are recorded as deferred revenue until earned.

Research and Development Prepaids and Accruals

As part of the process of preparing financial statements, we are required to estimate our expenses resulting from our obligation under contracts with vendors and consultants and clinical site agreements in connection with our research and development efforts. The financial terms of these contracts are subject to negotiations which vary contract to contract and may result in payment flows that do not match the periods over which materials or services are provided to us under such contracts.

Our objective is to reflect the appropriate research and development expenses in our financial statements by matching those expenses with the period in which services and efforts are expended. We account for these expenses according to the progress of our research and development efforts. We determine prepaid and accrual estimates through discussion with applicable personnel and outside service providers as to the progress or state of communication of clinical trials, or other services completed. We adjust our rate of research and development expense recognition if actual results differ from our estimates. We make estimates of our prepaid and accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known at that time. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of status and timing of services performed relative to the actual status and timing of services performed may vary and may result in us reporting amounts that are too high or too low for any particular period. Through December 31, 2018, there had been no material adjustments to our prior period estimates of prepaid and accruals for research and development expenses. Our research and development prepaids and accruals are dependent upon the timely and accurate reporting of contract research organizations and other third-party vendors.

Investments

Investments consist primarily of commercial paper, corporate bonds, U.S. Treasury securities and stock of a U.S. corporation. We invest in high-credit quality investments in accordance with our investment policy which minimizes the probability of loss.

Available-for-sale debt securities are carried at fair value as determined by quoted market prices, with the unrealized gains and losses, net of tax, reported as a separate component of stockholders deficit. Realized gains and losses are determined using the specific identification method and transactions are recorded on a settlement date basis in interest income (expense) and other, net. Investments with original maturities beyond three months at the date of purchase and which mature on, or less than twelve months from, the balance sheet date are classified as short-term. Investments with a maturity beyond twelve months from the balance sheet date are classified as long-term. We periodically review available-for-sale debt securities for other-than-temporary declines in fair value below the cost basis and whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. We evaluate, among other things, the duration and extent to which the fair value of a security is less than its cost; the financial condition of the issuer and any changes thereto; and our intent to sell, or whether we will more likely than not be required to sell, the security before recovery of our amortized cost basis. Any such declines in value judged to be other-than-temporary on available-for-sale securities are reported in other-than-temporary impairment of investment.

Prior to the fourth quarter of 2017, unrealized gains and losses in equity investments were reported as a separate component of stockholders equity. For the year ended December 31, 2017, we determined the decline in value for our investment in ContraVir common stock to be other-than temporary. As such, during the fourth quarter of 2017, we reclassified a loss of $1.2 million from accumulated other comprehensive loss, net in the Consolidated Balance Sheets to unrealized loss on equity investment in the Consolidated Statements of Operations and Comprehensive Loss. During 2018, changes in the fair value of equity investments were recorded to unrealzed loss on equity investment in the Consolidated Statements of Operations and Comprehensive Loss.

Valuation of Share-Based Compensation

We record the fair value of share-based awards issued as of the grant date as compensation expense. We recognize compensation expense over the requisite service period, which is equal to the vesting period.

Share-based compensation expense includes stock options, RSUs and employee stock purchase plan purchase rights and has been reported in our Consolidated Statements of Operations and Comprehensive Loss as follows (in thousands):

	Years Ended December 31,		
	2018	2017	2016
Income Statement Classification:			
Research and development expense	$5,343	$7,047	$7,137
General and administrative expense	7,731	9,063	9,086
Total stock-based compensation expense	$13,074	$16,110	$16,223

RSU compensation expense is based on the grant-date fair value of our common stock.

We calculate the fair value of share-based compensation awards using the Black-Scholes option-pricing model. The Black-Scholes option-pricing model requires the use of subjective assumptions, including volatility of our common stock, the expected term of our stock options, the risk-free interest rate for a period that approximates the expected term of our stock options and the fair value of the underlying common stock on the date of grant. In applying these assumptions, we considered the following factors:

- We have limited operating history to estimate the volatility of our common stock price. We calculate expected volatility based on a blend of company specific historical data and a group of similar publicly traded companies for which the historical information is available. For the purpose of identifying peer companies, we consider characteristics such as industry, length of trading history, similar vesting terms and in-the-money option status. We plan to continue to use the guideline peer group volatility information until the historical volatility of our common stock is relevant to measure expected volatility for future option grants.
- We use historical exercise data to estimate expected term.
- We determine the risk-free interest rate by reference to implied yields available from U.S. Treasury securities with a remaining term equal to the expected life assumed at the date of grant.
- The assumed dividend yield is based on our expectation of not paying dividends for the foreseeable future.
- We estimate forfeitures based on our historical analysis of actual stock option forfeitures.

The assumptions used in the Black-Scholes option-pricing model for the years ended December 31, 2018, 2017, and 2016 are set forth below:

Stock Options

	Years Ended December 31,		
	2018	2017	2016
Expected volatility	85.83%	85.51%	85.16%
Expected term (in years)	5.9	5.9	6.0
Weighted-average risk-free interest rate	2.52%	2.02%	1.70%
Expected dividend yield	—%	—%	—%
Weighted-average fair value per option	$3.43	$3.71	$5.62

Employee Stock Purchase Plan

	Years Ended December 31,		
	2018	2017	2016
Expected volatility	44.01%	77.18%	111.57%
Expected term (in years)	1.23	0.97	1.37
Weighted-average risk-free interest rate	2.56%	0.99%	0.75%
Expected dividend yield	—%	—%	—%
Weighted-average option value per share	$1.36	$2.65	$3.20

Utilization of Net Operating Loss Carryforwards

At December 31, 2018, we had net operating loss carryforwards for federal, state, and foreign tax purposes of approximately $465.3 million, $353.8 million and $0.4 million, respectively. At December 31, 2017, we had net operating loss carryforwards for federal, state, and foreign tax purposes of approximately $408.1 million, $319.9

million, and $0.4 million, respectively. In addition, we had tax credit carryforwards for federal tax purposes of approximately $18.4 million as of December 31, 2018, which begin to expire in 2022. The future utilization of net operating loss and tax credit carryforwards may be limited due to changes in ownership. In general, if we experience a greater than 50 percent aggregate change in ownership of certain significant stockholders or groups over a three-year period (a Section 382 ownership change), utilization of our pre-change net operating loss carryforwards is subject to an annual limitation under Section 382 of the Code (and similar state laws). The annual limitation generally is determined by multiplying the value of our stock at the time of such ownership change (subject to certain adjustments) by the applicable long-term tax-exempt rate. Such limitations may result in expiration of a portion of the pre-change net operating loss carryforwards before utilization and may be substantial. We have determined that a Section 382 ownership change occurred in

2002 and 2007 resulting in limitations of at least $64,000 and $762,000, respectively, of losses incurred prior to the respective ownership change dates. In addition, we have determined that another Section 382 ownership change occurred in 2013 with our initial public offering, our private placements and other transactions that have occurred since 2007, resulting in a limitation of at least $6.7 million of losses incurred prior to the ownership change date. We may also experience ownership changes in the future as a result of subsequent shifts in our stock ownership. Furthermore, under the Tax Act, federal net operating losses incurred in 2018 and in future years may be carried forward indefinitely, but the deductibility of such federal net operating losses is limited. It is uncertain if and to what extent various states will conform to the Tax Act. As a result, if we earn net taxable income, our ability to use our pre-change net operating loss carryforwards to offset United States federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us.

RESULTS OF OPERATIONS

Comparison of the Years Ended December 31, 2018 and December 31, 2017

The following table summarizes our results of operations for the years ended December 31, 2018 and December 31, 2017, together with the changes in those items in dollars and percentages (in thousands, except percentages):

	Years Ended December 31,		Dollar Change Increase/(Decrease)	% Change
	2018	2017		
Contract revenue	$7,216	$4,494	$2,722	60.6 %
Operating expenses:				
Research and development	55,239	49,448	5,791	11.7 %
General and administrative	23,582	27,148	(3,566)	(13.1)%
Total operating expenses	78,821	76,596	2,225	2.9 %
Loss from operations	(71,605)	(72,102)	497	(0.7)%
Other (expense) income:				
Unrealized loss on equity investment	(348)	(1,160)	812	(70.0)%
Interest income and other, net	2,479	2,278	201	8.8 %
Net loss	$(69,474)	$(70,984)	$1,510	(2.1)%

Contract Revenue

For the year ended December 31, 2018, contract revenue increased to $7.2 million compared to $4.5 million for the year ended December 31, 2017. The increase of $2.7 million, or 60.6%, was related to a increase in reimbursable expenses associated with our contract with BARDA.

Research and Development Expenses

For the year ended December 31, 2018, our research and development expenses increased to $55.2 million compared to $49.4 million for the year ended December 31, 2017. The increase of $5.8 million, or 11.7%, was primarily related to the following:

- an increase in oral brincidofovir clinical expenses of $3.2 million, which is comprised primarily of a $2.7 million increase related to the ongoing AdAPT clinical study and a $1.5 million increase of supporting bioequivalent and registry studies, primarily offset by a decrease of $1.0 million related to the completion of our AdVance study;
- an increase of $2.7 million in oral brincidofovir smallpox program expenses which primarily includes reimbursable BARDA contract expense;
- an increase of $1.7 million of supporting research and development expenses;
- an increase of $0.8 million related to IV brincidofovir development;

- a decrease of $1.5 million related to compensation expense; and
- a decrease of $1.3 million of development costs related to CMX521.

General and Administrative Expenses

For the year ended December 31, 2018, our general and administrative expenses decreased to $23.6 million compared to $27.1 million for the year ended December 31, 2017. The decrease of $3.6 million, or 13.1%, was primarily related to the following:

- a decrease of $2.3 million related to compensation expense;

- a decrease of $1.0 million in costs related to an indemnification claim settled in 2018; and
- a decrease of $0.3 million in global commercial readiness costs.

Interest Income and Other, net

For the year ended December 31, 2018, our interest income and other, net was $2.5 million compared to interest income of $2.3 million for the year ended December 31, 2017. The increase of $0.2 million was attributable to higher interest rates offset by $0.4 million of realized losses on the sale of short-term investments.

Unrealized Loss on Equity Investment

For the year ended December 31, 2018, unrealized loss on equity investment was $0.3 million compared to an unrealized loss on equity investment of $1.2 million for the year ended December 31, 2017. These unrealized losses relate to the decrease in value of our investment in ContraVir common stock.

Comparison of the Years ended December 31, 2017 and December 31, 2016

The following table summarizes our results of operations for the years ended December 31, 2017 and December 31, 2016, together with the changes in those items in dollars and percentages (in thousands, except for percentages):

	Years Ended December 31,		Dollar Change Increase/(Decrease)	% Change
	2017	2016		
Contract revenue	$4,494	$5,702	$(1,208)	(21.2)%
Operating expenses:				
Research and development	49,448	58,647	(9,199)	(15.7)%
General and administrative	27,148	25,007	2,141	8.6 %
Total operating expenses	76,596	83,654	(7,058)	(8.4)%
Loss from operations	(72,102)	(77,952)	5,850	(7.5)%
Other (expense) income:				
Unrealized loss on equity investment	(1,160)	—	(1,160)	*
Interest income	2,278	1,562	716	45.8 %
Net loss	$(70,984)	$(76,390)	$5,406	(7.1)%

* Not meaningful or not calculable

Contract Revenue

For the year ended December 31, 2017, contract revenue decreased to $4.5 million compared to $5.7 million for the year ended December 31, 2016. The decrease of $1.2 million, or 21.2%, was related to a decrease in reimbursable expenses associated with our contract with BARDA.

Research and Development Expenses

For the year ended December 31, 2017, our research and development expenses decreased to $49.4 million compared to $58.6 million for the year ended December 31, 2016. The decrease of $9.2 million, or 15.7%, was primarily related to the following:

- a decrease in oral brincidofovir clinical expenses of $6.2 million, which is comprised primarily of an $8.7 million decrease related to the completion of our Phase 3 SUPPRESS and AdVise trials and the closeout of our SUSTAIN

and SURPASS clinical trials, and a $0.6 million decrease in our expanded access programs, primarily offset by an increase of $1.8 million related to start-up activities for our AdAPT study and an increase of $1.2 million related to conduct of the AdVance study;

- a decrease of $1.4 million in oral brincidofovir drug manufacturing costs;
- a decrease of $1.9 million related to compensation expense;
- a decrease of $0.9 million related to reimbursable BARDA contract expenses; and
- a decrease of $0.8 million in supporting research and development expenses; offset by

- an increase of approximately $2.4 million mainly related to our development of an IV formulation of brincidofovir, development of CMX521, our clinical candidate for norovirus, and other early stage compounds.

General and Administrative Expenses

For the year ended December 31, 2017, our general and administrative expenses increased to $27.1 million compared to $25.0 million for the year ended December 31, 2016. The increase of $2.1 million, or 8.6%, was primarily related to the following:

- an increase of $2.0 million in global commercial readiness costs;
- an increase of $1.0 million in costs related to an indemnification claim; offset by
- a decrease of $0.6 million related to compensation expense.

Interest Income

For the year ended December 31, 2017, our interest income was $2.3 million compared to interest income of $1.6 million for the year ended December 31, 2016. The increase of $0.7 million was attributable to higher interest rates.

Unrealized Loss on Equity Investment

For the year ended December 31, 2017, unrealized loss on equity investment was $1.2 million related to the other-than-temporary-impairment write-down in value of our investment in ContraVir common stock. We recorded no other-than-temporary impairment of investment for the year ended December 31, 2016.

LIQUIDITY AND CAPITAL RESOURCES

We have incurred losses since our inception in 2000 and, as of December 31, 2018, we had an accumulated deficit of $556.3 million. We anticipate that we will continue to incur losses for at least the next several years. In connection with our ongoing AdAPT study, our IV brincidofovir trials and our smallpox program, we have seen an increase in expenses. We currently expect research and development expenses to remain consistent in 2019 compared to 2018, and we will need additional capital in the future to fund our operations, which we may obtain through one or more equity offerings, debt financings, government or other third-party funding, strategic alliances and licensing or collaboration arrangements.

On November 8, 2017, the Company entered into an at-the-market (ATM) sales agreement with Cowen and Company, LLC to sell up to $75 million of the Company’s common stock under a shelf registration statement filed in November 2017. As of February 26, 2019, the Company had sold an aggregate of 2.8 million shares of common stock at a weighted average price per share of $4.00 for $10.9 million of proceeds net of commissions.

We cannot assure you that adequate funding will be available on terms acceptable to us, if at all. Any additional equity financings will be dilutive to our stockholders and any additional debt may involve operating covenants that may restrict our business. If adequate funds are not available through these means, we may be required to curtail significantly one or more of our research or development programs, our pre-launch expenses, and any launch and other commercialization expenses for any of our products that may receive marketing approval. We cannot assure you that we will successfully develop or commercialize our products under development or that our products, if successfully developed, will generate revenues sufficient to enable us to earn a profit.

We believe that our existing cash, cash equivalents, and short-term investments will enable us to fund our current operating expenses and capital requirements for at least the next 12 months. Such operating and capital requirements

do not contemplate incremental expenses associated with a full scale commercial launch of brincidofovir. However, changing circumstances beyond our control may cause us to consume capital more rapidly than we currently anticipate.

Since our inception through December 31, 2018, we have funded our operations principally with $606.1 million from the sale of common stock and preferred stock, $37.4 million of research funding from our various National Institute of Allergy and Infectious Diseases awards, $63.4 million in revenue from our BARDA contract, debt financings totaling $21.0 million, $17.5 million of licensing revenue, and $14.8 million from stock option and warrant exercises and purchases under our Employee Stock Purchase Plan (ESPP). As of December 31, 2018, we had capital available to fund operations of approximately $186.5 million. Cash in excess of immediate requirements is invested in accordance with our investment policy, primarily with a view to liquidity and capital preservation.

Cash Flows

The following table sets forth the significant sources and uses of cash for the periods (in thousands):

	Years Ended December 31,		
Cash sources and uses:	2018	2017	2016
Net cash used in operating activities	$(53,725)	$(50,125)	$(63,815)
Net cash provided by investing activities	105,095	16,431	94,065
Net cash provided by financing activities	11,188	779	608
Net increase (decrease) in cash and cash equivalents	$62,558	$(32,915)	$30,858

Operating Activities

Net cash used in operating activities of $53.7 million for the year ended December 31, 2018 was primarily the result of our $69.5 million net loss, offset by the change in operating assets and liabilities and the add-back of non-cash expenses. Non-cash expenses included add-backs of $13.1 million for stock based compensation, $0.9 million of depreciation of property and equipment, $0.4 million for a loss on the sale of investments, and $0.3 million for a loss on equity investment, offset by $0.9 million of amortization of discount/premium on investments. The change in operating assets and liabilities includes a decrease in prepaid expenses and other assets of $0.6 million and a decrease of $1.4 million in accounts receivable.

Net cash used in operating activities of $50.1 million for the year ended December 31, 2017 was primarily the result of our $71.0 million net loss, offset by the change in operating assets and liabilities and the add-back of non-cash expenses of $16.1 million for stock based compensation, $1.2 million for an impairment loss on financial assets and $1.1 million of depreciation of property and equipment. The change in operating assets and liabilities includes an increase in accounts payable and accrued liabilities of $3.1 million, offset by an increase in prepaid expenses and other assets of $0.2 million and an increase of $0.1 million in accounts receivable.

Net cash used in operating activities of $63.8 million for the year ended December 31, 2016 was primarily the result of our $76.4 million net loss and the change in operating assets and liabilities, offset by the add-back of non-cash expenses of $16.2 million for stock based compensation, $1.2 million of amortization of premiums on investments and $1.1 million of depreciation of property and equipment. The change in operating assets and liabilities includes a decrease in accounts payable and accrued liabilities of $10.1 million, offset by a decrease in prepaid expenses and other assets of $3.2 million and a decrease of $0.9 million in accounts receivable due to a decrease in reimbursable expenses related to our contract with BARDA.

Investing Activities

Net cash provided by investing activities of $105.1 million during the year ended December 31, 2018 was primarily the result of maturities and sale of short-term investments, offset by purchases of short-term and long-term investments. Net cash provided by investing activities of $16.4 million during the year ended December 31, 2017 was primarily the result of maturities and sales of short-term investments, offset by purchases of long-term investments. Net cash provided by investing activities of $94.1 million during the year ended December 31, 2016 was primarily the result of maturities of short-term investments, offset by purchases of short-term and long-term investments.

Financing Activities

Net cash provided by financing activities of $11.2 million for the year ended December 31, 2018 was primarily the result of $10.9 million in proceeds from the issuance of common stock, $0.7 million from the exercise of stock options and purchases under the ESPP, offset by $0.4 million in payments of deferred offering costs. Net cash provided by

financing activities of $0.8 million for the year ended December 31, 2017 was primarily the result of $0.8 million from the exercise of stock options and purchases under the ESPP. Net cash provided by financing activities of $0.6 million for the year ended December 31, 2016 was primarily the result of $0.6 million from the exercise of stock options and purchases under the ESPP.

Future Funding Requirements

To date, we have not generated any revenue from product sales. We do not know when, or if, we will generate any revenue from product sales. We do not expect to generate significant revenue from product sales unless and until we obtain regulatory approval of and commercialize brincidofovir or any of our other product candidates. At the same time, we expect our expenses to increase

in connection with our ongoing development activities, particularly as we continue the research, development and clinical trials of, and seek regulatory approval for, our product candidates. Furthermore, subject to obtaining regulatory approval of any of our product candidates, we expect to incur significant commercialization expenses for product sales, marketing, manufacturing and distribution. We anticipate that we will need substantial additional funding in connection with our continuing operations. Based upon our current operating plan, we believe that our existing cash, cash equivalents and short-term investments, will enable us to fund our operating expenses and capital requirements for at least the next 12 months. We have based our estimates on assumptions that may prove to be wrong, and we may use our available capital resources sooner than we currently expect. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenditures necessary to complete the development of our product candidates.

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

- the willingness of the FDA and/or foreign regulators to accept the results from our AdAPT study, as well as our other completed and planned clinical and preclinical studies and other work, as the basis for review and approval of brincidofovir for the treatment of AdV infection;
- the progress, costs, results and timing of future clinical trials of brincidofovir for other potential indications, including prevention of multiple DNA virus infections and treatment of AdV, BKV and smallpox;
- the willingness of the FDA and/or foreign regulators to accept clinical and preclinical studies and other work, as the basis for review and approval of brincidofovir for other potential indications;
- the outcome, costs and timing of seeking and obtaining FDA and any other regulatory approvals;
- the ability to continue to receive government funding;
- the achievement of milestones under our agreement with ContraVir;
- the number and characteristics of product candidates that we pursue, including our product candidates in preclinical development;
- the ability of our product candidates to progress through clinical development successfully;
- our need to expand our research and development activities;
- the costs associated with securing, establishing and maintaining commercialization and manufacturing capabilities;
- the costs of acquiring, licensing or investing in businesses, products, product candidates and technologies;
- our ability to maintain, expand and defend the scope of our intellectual property portfolio, including the amount and timing of any payments we may be required to make, or that we may receive, in connection with the licensing, filing, prosecution, defense and enforcement of any patents or other intellectual property rights;
- our need and ability to hire additional management and scientific and medical personnel;
- the effect of competing technological and market developments;
- our need to implement additional internal systems and infrastructure, including financial and reporting systems; and
- the economic and other terms, timing and success of our existing licensing arrangements and any collaboration, licensing or other arrangements into which we may enter in the future.

Until such time, if ever, as we can generate substantial revenue from product sales, we expect to finance our cash needs through a combination of equity offerings, debt financings, government or other third-party funding, marketing and distribution arrangements, or other collaborations, strategic alliances or licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our common stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through government or other third-party funding, marketing and distribution arrangements or other collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research

programs or product candidates or to grant licenses on terms that may not be favorable to us.

CONTRACTUAL OBLIGATIONS AND COMMITMENTS

The following table summarizes our contractual obligations at December 31, 2018 (in thousands):

	Total	Less Than 1 Year	1 – 3 Years	3 – 5 Years	More Than 5 Years
Operating leases (1)	$1,818	$ 786	$ 1,032	$ —	$ —
Total	$1,818	$ 786	$ 1,032	$ —	$ —

(1) Consists of our corporate headquarters lease encompassing 24,862 square feet of office space that expires in February 2021, and our laboratory leases encompassing a total of approximately 10,274 square feet which are located in Durham and Research Triangle Park, North Carolina and expire in July 2021 and August 2021, respectively.

In addition to the amounts set forth in the table above, we have payment obligations under license agreements that are contingent upon future events such as our achievement of specified development, regulatory and commercial milestones. We will be required to make additional payments when certain milestones are achieved and we are obligated to pay royalties based on future product sales. As of December 31, 2018, we were unable to estimate the timing or likelihood of achieving the milestones or making future product sales and, therefore, any related payments are not included in the table above. In connection with the development and commercialization of brincidofovir and CMX157 (which we have licensed to ContraVir Pharmaceuticals), in addition to royalties on product sales, we could be required to pay UC up to an aggregate of $3.4 million in milestone payments, assuming the achievement of all applicable milestone events under the license agreement. Under our license agreement with the University of Michigan, we are required to pay minimum royalties from 2024 through the expiration of the last licensed issued patent (which we estimate to be $20,000 in the year 2024), but any additional royalties that may be payable under the University of Michigan agreement are not estimable.

Additionally, we enter into contracts in the normal course of business with CROs for clinical trials and clinical supply manufacturing and with vendors for preclinical research studies and other services and products for operating purposes, which generally provide for termination or cancellation within 30 days of notice, and therefore are not included in the table above. We also have agreements with our executive officers that require the funding of specific payments, if certain events occur, such as a change in control or the termination of employment without cause. These potential payment obligations are not included in the table above.

Off-Balance Sheet Arrangements

During the periods presented, we did not have, nor do we currently have, any off-balance sheet arrangements as defined under SEC rules.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 10.0% change in interest rates would not have a material effect on the fair market value of our portfolio. Accordingly, we would not expect our operating results or cash flows to be affected to any significant degree by the effect of a sudden change in market interest rates on our investment portfolio.

We do not believe that our cash, cash equivalents and available-for-sale investments have significant risk of default or illiquidity. While we believe our cash and cash equivalents and available-for-sale investments do not contain excessive risk, we cannot provide absolute assurance that in the future our investments will not be subject to adverse

changes in market value. In addition, we maintain significant amounts of cash and cash equivalents at one or more financial institutions that are in excess of federally insured limits.

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation has had a material effect on our results of operations for the years ended December 31, 2018 or 2017.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

	Page
Reports of Independent Registered Public Accounting Firm	67
Consolidated Balance Sheets as of December 31, 2018 and 2017	69
Consolidated Statements of Operations and Comprehensive Loss for the Years Ended December 31, 2018, 2017 and 2016	70
Consolidated Statements of Stockholders' Equity (Deficit) for the Years Ended December 31, 2018, 2017 and 2016	71
Consolidated Statements of Cash Flows for the Years Ended December 31, 2018, 2017 and 2016	72
Notes to Consolidated Financial Statements	73

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Shareholders and the Board of Directors of Chimerix, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Chimerix, Inc. (the Company) as of December 31, 2018 and 2017, the related consolidated statements of operations and comprehensive loss, stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2018, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2018 and 2017, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2018, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2018, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) and our report dated March 5, 2019 expressed an unqualified opinion thereon.

Basis for Opinion

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

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

We have served as the Company's auditor since 2008.

/s/ Ernst & Young LLP
Raleigh, North Carolina
March 5, 2019

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Shareholders and the Board of Directors of Chimerix, Inc.

Opinion on Internal Control over Financial Reporting

We have audited Chimerix, Inc.'s internal control over financial reporting as of December 31, 2018, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, Chimerix, Inc. (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2018, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2018 and 2017, the related consolidated statements of operations and comprehensive loss, stockholders' equity (deficit), and cash flows for each of the three years in the period ended December 31, 2018, and the related notes and our report dated March 5, 2019 expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the 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 audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ Ernst & Young LLP
Raleigh, North Carolina
March 5, 2019

CHIMERIX, INC.
CONSOLIDATED BALANCE SHEETS
(in thousands, except share and per share data)

	December 31,	
	2018	2017
ASSETS		
Current assets:		
Cash and cash equivalents	$81,106	$18,548
Short-term investments, available-for-sale	105,424	132,972
Accounts receivable	330	1,682
Prepaid expenses and other current assets	2,598	3,331
Total current assets	189,458	156,533
Long-term investments	—	76,731
Property and equipment, net of accumulated depreciation	1,210	1,894
Other long-term assets	46	72
Total assets	$190,714	$235,230
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$4,691	$3,812
Accrued liabilities	8,275	9,384
Total current liabilities	12,966	13,196
Lease-related obligations	144	224
Total liabilities	13,110	13,420
Stockholders’ equity:		
Preferred stock, $0.001 par value, 10,000,000 shares authorized at December 31, 2018 and 2017; no shares issued and outstanding as of December 31, 2018 and 2017	—	—
Common stock, $0.001 par value; 200,000,000 shares authorized at December 31, 2018 and 2017; 50,735,279 and 47,505,532 shares issued and outstanding at December 31, 2018 and 2017, respectively	51	47
Additional paid-in capital	733,907	709,514
Accumulated other comprehensive loss, net	(92)	(963)
Accumulated deficit	(556,262)	(486,788)
Total stockholders’ equity	177,604	221,810
Total liabilities and stockholders’ equity	$190,714	$235,230

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

CHIMERIX, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(in thousands, except share and per share data)

	Years Ended December 31,		
	2018	2017	2016
Contract revenue	$7,216	$4,494	$5,702
Operating expenses:			
Research and development	55,239	49,448	58,647
General and administrative	23,582	27,148	25,007
Total operating expenses	78,821	76,596	83,654
Loss from operations	(71,605)	(72,102)	(77,952)
Other (expense) income:			
Unrealized loss on equity investment	(348)	(1,160)	—
Interest income and other, net	2,479	2,278	1,562
Net loss	(69,474)	(70,984)	(76,390)
Other comprehensive loss:			
Unrealized gain (loss) on investments, net	871	(523)	324
Comprehensive loss	$(68,603)	$(71,507)	$(76,066)
Per share information:			
Net loss, basic and diluted	$(1.43)	$(1.51)	$(1.65)
Weighted-average shares outstanding, basic and diluted	48,593,435	46,963,430	46,267,064

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

CHIMERIX, INC.
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY (DEFICIT)
(in thousands)

	Common Stock	Additional Paid-in Capital	Accumulated Other Comprehensive Gain (Loss)	Accumulated Deficit	Total Stockholders' Equity (Deficit)
Balance, December 31, 2015	$ 46	$ 675,591	$ (764)	$ (339,414)	$ 335,459
Share-based compensation	—	16,223	—	—	16,223
Exercise of stock options	—	168	—	—	168
Employee stock purchase plan purchases	—	440	—	—	440
Comprehensive loss:					
Unrealized gain on investments, net	—	—	324	—	324
Net loss	—	—	—	(76,390)	(76,390)
Total comprehensive loss					(76,066)
Balance, December 31, 2016	46	692,422	(440)	(415,804)	276,224
Share-based compensation	1	16,109	—	—	16,110
Exercise of stock options	—	121	—	—	121
Employee stock purchase plan purchases	—	712	—	—	712
University of Michigan stock issuance	—	150	—	—	150
Comprehensive loss:					
Unrealized loss on investments, net	—	—	(523)	—	(523)
Net loss	—	—	—	(70,984)	(70,984)
Total comprehensive loss					(71,507)
Balance, December 31, 2017	47	709,514	(963)	(486,788)	221,810
Share-based compensation	1	13,073	—	—	13,074
Exercise of stock options	—	115	—	—	115
Employee stock purchase plan purchases	—	608	—	—	608
Issuance of common stock, net of issuance costs	3	10,597	—	—	10,600
Comprehensive loss:					
Unrealized gain on investments, net	—	—	871	—	871
Net loss	—	—	—	(69,474)	(69,474)
Total comprehensive loss					(68,603)
Balance, December 31, 2018	$ 51	$ 733,907	$ (92)	$ (556,262)	$ 177,604

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

CHIMERIX, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	Years Ended December 31,		
	2018	2017	2016
Cash flows from operating activities:			
Net loss	$(69,474)	$(70,984)	$(76,390)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation of property and equipment	860	1,091	1,063
Amortization of discount/premium on investments	(852)	(5)	1,223
Share-based compensation	13,074	16,110	16,223
Loss on sale of investments	378	—	—
Unrealized loss on equity investment	348	1,160	—
Amortization of lease-related obligations	(59)	(319)	132
Changes in operating assets and liabilities:			
Accounts receivable	1,352	(83)	861
Prepaid expenses and other assets	643	(168)	3,215
Accounts payable and accrued liabilities	5	3,073	(10,142)
Net cash used in operating activities	(53,725)	(50,125)	(63,815)
Cash flows from investing activities:			
Purchases of property and equipment	(181)	(151)	(841)
Purchases of short-term investments	(125,611)	—	(23,992)
Purchases of long-term investments	(6,031)	(162,613)	(79,381)
Proceeds from sales of short-term investments	111,178	13,500	—
Proceeds from maturities of short-term investments	125,740	165,695	198,279
Net cash provided by investing activities	105,095	16,431	94,065
Cash flows from financing activities:			
Proceeds from exercise of stock options	115	121	168
Proceeds from employee stock purchase plan	608	712	440
Proceeds from issuance of common stock, net of commissions	10,867	—	—
Payments of deferred offering costs	(402)	(54)	—
Net cash provided by financing activities	11,188	779	608
Net increase (decrease) in cash and cash equivalents	62,558	(32,915)	30,858
Cash and cash equivalents:			
Beginning of period	18,548	51,463	20,605
End of period	$81,106	$18,548	$51,463
Supplemental disclosure of cash flow information			
Non-cash addition to deferred offering costs	$22	$276	$—

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

CHIMERIX, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

Note 1. The Business and Summary of Significant Accounting Policies

Description of Business

Chimerix, Inc. (the Company) is a biopharmaceutical company committed to discovering, developing and commercializing medicines that improve outcomes for immunocompromised patients. The Company was founded in 2000 based on the promise of its proprietary lipid conjugate technology to unlock the potential of some of the most broad-spectrum antivirals by enhancing their antiviral activity and safety profiles in convenient dosing regimens. The Company's lead compound, brincidofovir, is in development as an oral and intravenous (IV) formulation for the prevention and treatment of DNA viruses, including smallpox, adenoviruses, and the human herpesviruses. In addition, the Company has an active discovery program focusing on viral targets for which limited or no therapies are currently available.

Basis of Presentation

The consolidated financial statements include the accounts of the Company, and its wholly owned subsidiaries. The accompanying consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America (GAAP). The preparation of the Company’s consolidated financial statements requires estimates and assumptions that affect the reported amounts of assets, liabilities, revenues and expenses, and the disclosure of contingent assets and liabilities in the consolidated financial statements and accompanying notes. Although these estimates are based on knowledge of current events and actions the Company may undertake in the future, actual results may ultimately differ from these estimates and assumptions.

Reclassifications

Certain prior period amounts in the accompanying consolidated financial statements have been reclassified to conform to the current year presentation. These reclassifications had no effect on previously reported net income or stockholders' equity (deficit).

Cash and Cash Equivalents

The Company considers any highly liquid instrument with an original maturity of three months or less at acquisition to be a cash equivalent. Cash equivalents consist of money market funds, U.S. Treasury securities, commercial paper, and corporate bonds.

Investments

Investments consist primarily of commercial paper, corporate bonds, U.S. Treasury securities and stock of a U.S. corporation. The Company invests in high-credit quality investments in accordance with its investment policy which minimizes the probability of loss.

Available-for-sale debt securities are carried at fair value as determined by quoted market prices, with the unrealized gains and losses, net of tax, reported as a separate component of stockholders equity. Realized gains and losses are determined using the specific identification method and transactions are recorded on a settlement date basis in interest income and other, net. For the year ended December 31, 2018, $0.4 million of realized losses were reclassified from accumulated other comprehensive loss, net in the Consolidated Balance Sheets to interest income and other, net in the

Consolidated Statements of Operations and Comprehensive Loss. Investments with original maturities beyond three months at the date of purchase and which mature on, or less than twelve months from, the balance sheet date are classified as short-term. Investments with a maturity beyond twelve months from the balance sheet date are classified as long-term.

The Company periodically reviews available-for-sale debt securities for other-than-temporary declines in fair value below the cost basis and whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. The Company evaluates, among other things, the duration and extent to which the fair value of a security is less than its cost; the financial condition of the issuer and any changes thereto; and the Company's intent to sell, or whether it will more likely than not be required to sell, the security before recovery of its amortized cost basis. The Company does not intend to sell, and is not likely to be required to sell, the available-for-sale debt securities in an unrealized loss position before recovery of the amortized cost bases of the debt securities, which may be maturity. Any such declines in value judged to be other-than-temporary on available-for-sale debt securities are reported in other-than-temporary impairment of investment.

For the year ended December 31, 2017, the Company determined the decline in value for its investment in ContraVir Pharmaceuticals (ContraVir) common stock to be other-than temporary. As such, during the fourth quarter of 2017, the Company reclassified a loss of $1.2 million from accumulated other comprehensive loss, net in the Consolidated Balance Sheets to unrealized loss on equity investment the Consolidated Statements of Operations and Comprehensive Loss. For the year ended December 31, 2018, the Company recorded $0.3 million, of unrealized loss related to the Company's investment in ContraVir common stock to unrealized loss on equity investment in the Consolidated Statements of Operations and Comprehensive Loss. The Company recognizes interest income on an accrual basis in interest income and other, net in the Consolidated Statements of Operations and Comprehensive Loss.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to concentrations of credit risk consist of cash, cash equivalents, short-term investments, long-term investments and accounts receivable. The Company is exposed to credit risk, subject to federal deposit insurance, in the event of default by the financial institutions holding its cash and cash equivalents to the extent of amounts recorded on the balance sheets. Accounts receivable represent amounts due from an agency of the federal government.

Accounts Receivable

Accounts receivable at December 31, 2018 and December 31, 2017 consisted of amounts billed under the Company’s contract with the Biomedical Advanced Research and Development Authority (BARDA). Receivables under the BARDA contract are recorded as qualifying research activities are conducted and invoices from the Company’s vendors are received. The Company carries its accounts receivable at cost less an allowance for doubtful accounts. On a periodic basis, the Company evaluates its accounts receivable and establishes an allowance based on its history of collections and write-offs and the current status of all receivables. The Company does not accrue interest on trade receivables. If accounts become uncollectible, they will be written off through a charge to the allowance for doubtful accounts. The Company has not recorded a charge to allowance for doubtful accounts as management believes all receivables are fully collectible.

Fair Value of Financial Instruments

The carrying amounts of certain financial instruments, including accounts receivable, accounts payable and accrued expenses approximate their fair values due to the short-term nature of such instruments.

For assets and liabilities recorded at fair value, it is the Company’s policy to maximize the use of observable inputs and minimize the use of unobservable inputs when developing fair value measurements, in accordance with the fair value hierarchy. Fair value measurements for assets and liabilities where there exists limited or no observable market data are based primarily upon estimates and are often calculated based on the economic and competitive environment, the characteristics of the asset or liability and other factors. Therefore, fair value measurements cannot be determined with precision and may not be realized in an actual sale or immediate settlement of the asset or liability. Additionally, there may be inherent weaknesses in any calculation technique and changes in the underlying assumptions used, including discount rates and estimates of future cash flows, could significantly affect the calculated current or future fair values. The Company utilizes fair value measurements to record fair value adjustments to certain assets and liabilities and to determine fair value disclosures.

The Company groups assets and liabilities at fair value in three levels, based on the markets in which the assets and liabilities are traded and the reliability of the assumptions used to determine fair value. The determination of where an asset or liability falls in the hierarchy requires significant judgment. These levels are:

- Level 1 — Valuations based on unadjusted quoted prices in active markets for identical assets or liabilities that the Company has the ability to access.
- Level 2 — Valuations based on quoted prices for similar assets or liabilities in active markets, quoted prices for identical or similar assets or liabilities in markets that are not active, and models for which all significant inputs are observable, either directly or indirectly.
- Level 3 — Valuations based on inputs that are unobservable and significant to the overall fair value measurement.

At December 31, 2018, the Company had cash equivalents, including money market funds and U.S. Treasury securities, and short-term investments, including U.S. Treasury securities. At December 31, 2017, the Company had cash equivalents, including money market funds, and short-term and long-term investments, including U.S. Treasury securities, whose value is based on using quoted market prices. Accordingly, these securities are classified as Level 1.

At December 31, 2018 and 2017, the Company had short-term investments, including stock of a U.S. corporation. The Company's investment in ContraVir Pharmaceuticals (ContraVir) common stock was categorized as a Level 1 asset and had a value based on ContraVir's common stock value at December 31, 2018 and 2017. For the twelve months ended December 31, 2018 and 2017, the Company recorded $0.3 million and $1.2 million, respectively, of unrealized loss related to the Company's investment in ContraVir common stock to unrealized loss on equity investment in the Consolidated Statements of Operations and Comprehensive Loss. For the twelve months ended December 31, 2016, the Company recorded $0.2 million of unrealized loss related to the Company's investment in ContraVir common stock to unrealized gain (loss) on investments, net in the Consolidated Statements of Operations and Comprehensive Loss.

At December 31, 2018, the Company had cash equivalents, including commercial paper and corporate bonds, and short-term investments including, commercial paper and corporate bonds. At December 31, 2017, the Company had cash equivalents including commercial paper. As quoted prices are not available for these securities, they are valued using independent pricing models or other model-based valuation techniques such as the present value of future cash flows, adjusted for the security’s credit rating, prepayment assumptions and other factors such as credit loss assumptions. Accordingly, these securities are classified as Level 2.

There was no material re-measurement to fair value of financial assets and liabilities that are not measured at fair value on a recurring basis. For additional information regarding the Company's investments, please refer to Note 2, "Investments."

Below is a table that presents information about certain assets measured at fair value on a recurring basis (in thousands):

	Total	Fair Value Measurements December 31, 2018 Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	
Cash equivalents					
Money market funds	$30,726	$ 30,726	$ —	$	—
U.S. Treasury securities	11,482	11,482	—	—	
Commercial paper	29,677	—	29,677	—	
Corporate bonds	4,008	—	4,008	—	
Total cash equivalents	75,893	42,208	33,685	—	
Short-term investments					
U.S. Treasury securities	12,589	12,589	—	—	
Common stock of U.S. corporation	38	38	—	—	
Commercial paper	60,114	—	60,114	—	
Corporate bonds	32,683	—	32,683	—	
Total short-term investments	105,424	12,627	92,797	—	
Total assets	$181,317	$ 54,835	$ 126,482	$	—

	Total	Fair Value Measurements December 31, 2017 Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Cash equivalents				
Money market funds	$10,816	$ 10,816	$ —	$ —
Commercial paper	3,995	—	3,995	—
Total cash equivalents	14,811	10,816	3,995	—
Short-term investments				
U.S. Treasury securities	132,586	132,586	—	—
Common stock of U.S. corporation	386	386	—	—
Total short-term investments	132,972	132,972	—	—
Long-term investments				
U.S. Treasury securities	76,731	76,731	—	—
Total long-term investments	76,731	76,731	—	—
Total assets	$224,514	$ 220,519	$ 3,995	$ —

Prepaid Expenses and Other Current Assets

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

	December 31,	
	2018	2017
Prepaid research and development expenses	$1,071	$1,138
Interest receivable	259	601
Prepaid insurance	382	481
Other prepaid expenses and current assets	886	1,111
Total prepaid expenses and other current assets	$2,598	$3,331

Property and Equipment

Property and equipment are stated at cost, less accumulated depreciation. Depreciation is determined on a straight-line basis over the estimated useful lives of the assets, which generally range from three to five years. Leasehold improvements are amortized over the shorter of the useful life of the asset or the term of the related lease. Maintenance and repairs are charged against expense as incurred.

Impairment of Property and Equipment

The Company evaluates property and equipment for impairment whenever events or changes in circumstances indicate that the carrying value of an asset may not be recoverable. If the estimated future cash flows (undiscounted and without interest charges) from the use of an asset are less than the carrying value, a write-down would be recorded to reduce the related asset to its estimated fair value. To date, no such write-downs have occurred.

Deferred Lease Obligations

The Company recognizes rent expense on a straight-line basis over the non-cancelable term of its operating lease and records the difference between cash rent payments and the recognition of rent expense as a deferred rent liability. The Company also records landlord-funded lease incentives, such as reimbursable leasehold improvements, as a deferred

rent liability, which is amortized as a reduction of rent expense over the non-cancelable term of its operating lease.

Accrued Liabilities

Accrued liabilities consisted of the following (in thousands):

	December 31,	
	2018	2017
Accrued compensation	$2,469	$3,678
Accrued research and development expenses	4,525	3,384
Accrued indemnification claim	—	1,000
Other accrued liabilities	1,281	1,322
Total accrued liabilities	$8,275	$9,384

Revenue Recognition

Policy

The Company's revenues generally consist of (i) contract revenue - revenue generated under federal contracts, and (ii) collaboration and licensing revenue - revenue related to non-refundable upfront fees, royalties and milestone payments earned under license agreements. Revenue is recognized in accordance with the criteria outlined in Accounting Standards Codification (ASC) 606 issued by the Financial Accounting Standards Board (FASB). Following this accounting pronouncement, a five-step approach is applied for recognizing revenue, including (1) identify the contract with a customer; (2) identify the performance obligations in the contract; (3) determine the transaction price; (4) allocate the transaction price to the performance obligations in the contract; and (5) recognize revenue when, or as, the entity satisfies a performance obligation.

Biomedical Advanced Research and Development Authority (BARDA)

In February 2011, the Company entered into a contract with BARDA for the advanced development of brincidofovir as a medical countermeasure in the event of a smallpox release. Under the contract, the Company may receive up to $75.8 million in expense reimbursement and $5.3 million in fees over the performance of 1 base segment and 4 option segments. Exercise of each option segment is solely at the discretion of BARDA. Currently, option segments 1 through 3 have been exercised. The Company assessed the services in accordance with the authoritative guidance and concluded that there is a potential of 5 separate contracts (1 base segment and four option segments) within this agreement, each of which has a single performance obligation. The transaction price for each segment, based on the transaction price as defined in each segment contract, is allocated to the single performance obligation for each contract. The transaction price is recognized over time by measuring the progress toward complete satisfaction of the performance obligation. The progress toward complete satisfaction is estimated based on the costs incurred to date relative to the total estimated costs per the terms of each contract. The Company typically invoices BARDA monthly as costs are incurred. The base segment and first option segment were completed prior to adoption of ASC 606. The Company is currently performing under the second and third option segments of the contract during which the Company may receive up to a total of $23.9 million and $14.1 million in expense reimbursement and fees, respectively. The second option segment is scheduled to end on August 1, 2019 and the third option segments is scheduled to end on March 30, 2019.

ContraVir Pharmaceuticals

The Company entered into a license agreement with ContraVir on December 17, 2014 for the development and commercialization of CMX157 for certain antiviral indications. The Company is eligible to receive up to approximately $20 million in clinical, regulatory and initial commercial milestones as well as royalties and additional milestones based on commercial sales. The Company assessed the agreement in accordance with the authoritative

guidance and concluded that the ContraVir contract includes multiple performance obligations, which had all been satisfied in 2015 prior to the adoption of ASC 606. The ContraVir contract has one fixed and several variable transaction amounts. The fixed fee portion of the contract was for the license to CMX157 rights. The Company recognized revenue for the fixed fee portion of the contract in 2015 when the performance obligations were satisfied. All variable transaction amounts, which relate to clinical, regulatory and commercial milestones as well as royalties and milestones based on commercial sales, are fully constrained. The Company will begin recognizing revenue on the variable transaction amounts when those transaction amounts are no longer fully constrained.

Research and Development Prepaids and Accruals

As part of the process of preparing financial statements, the Company is required to estimate its expenses resulting from its

obligation under contracts with vendors and consultants and clinical site agreements in connection with its research and development efforts. The financial terms of these contracts are subject to negotiations which vary contract to contract and may result in payment flows that do not match the periods over which materials or services are provided to the Company under such contracts.

The Company's objective is to reflect the appropriate research and development expenses in its financial statements by matching those expenses with the period in which services and efforts are expended. The Company accounts for these expenses according to the progress of its research and development efforts. The Company determines prepaid and accrual estimates through discussion with applicable personnel and outside service providers as to the progress or state of communication of clinical trials, or other services completed. The Company adjusts its rate of research and development expense recognition if actual results differ from its estimates. The Company makes estimates of its prepaid and accrued expenses as of each balance sheet date in its financial statements based on facts and circumstances known at that time. Although the Company does not expect its estimates to be materially different from amounts actually incurred, its understanding of status and timing of services performed relative to the actual status and timing of services performed may vary and may result in the Company reporting amounts that are too high or too low for any particular period. Through December 31, 2018, there had been no material adjustments to the Company's prior period estimates of prepaid and accruals for research and development expenses. The Company's research and development prepaids and accruals are dependent upon the timely and accurate reporting of contract research organizations and other third-party vendors.

Research and Development Expenses

Major components of research and development costs include cash compensation, stock based compensation, pre-clinical studies, clinical trial and related clinical manufacturing, drug development, materials and supplies, legal, regulatory compliance, and fees paid to consultants and other entities that conduct certain research and development activities on the Company's behalf. Research and development costs, including upfront fees and milestones paid to contract research organizations, are expensed as goods are received or services rendered. Costs incurred in connection with clinical trial activities for which the underlying nature of the activities themselves do not directly relate to active research and development, such as costs incurred for market research and focus groups linked to clinical strategy as well as costs to build the Company's brand, are not included in research and development costs but are reflected as general and administrative costs.

Unrealized Loss on Equity Investment

As of December 31, 2018, unrealized loss on equity investment consists of the decrease in fair value of our investment in ContraVir common stock. As of December 31, 2017, unrealized loss on equity investment consists of the write-down in fair value of our investment in ContraVir common stock which was judged to be other-than-temporarily impaired.

Interest Income and Other, Net

Interest income and other, net primarily includes interest earned on short-term and long-term investments and realized gains on the sale of short-term investments.

Income Taxes

Deferred tax assets and liabilities are determined based on differences between the financial and tax reporting bases of assets and liabilities and are measured using enacted tax rates and laws that are expected to be in effect when the differences are expected to reverse. Valuation allowances are established when the Company determines that it is

more likely than not that some portion of a deferred tax asset will not be realized. The Company has incurred operating losses from April 7, 2000 (inception) through December 31, 2018, and therefore has not recorded any current provision for income taxes.

Additionally, the Company recognizes the tax benefit from an uncertain tax position only if it is more likely than not that the tax position will be sustained on examination by the taxing authorities based on the technical merits of the position. The tax benefit recognized in the financial statements for a particular tax position is based on the largest benefit that is more likely than not to be realized upon settlement. Accordingly, the Company establishes reserves for uncertain tax positions.

The FASB Staff Q&A, Topic 740, No. 5, Accounting for Global Intangible Low-Taxed Income (GILTI), states that an entity can make an accounting policy election to either recognized deferred taxes for temporary basis differences expected to reverse as GILTI in future years or to provide for the tax expense related to GILTI in the year the tax is incurred as a period expense only. The Company has elected to account for GILTI as a period expense in the year the tax is incurred.

Share-Based Compensation

The Company measures and recognizes compensation expense for all share-based payment awards made to employees and directors, including employee stock options, restricted stock units and the employee stock purchase plan purchase rights, based on estimated fair values. The fair value of employee stock options and employee stock purchase plan purchase rights is estimated on the grant date using the Black-Scholes valuation model. The grant-date fair value for restricted stock units is based upon the market price of the Company's common stock on the date of the grant. The value of the portion of the award that is ultimately expected to vest is recorded as expense over the requisite service periods. For performance-based awards compensation cost is recognized when it is probable that the performance criteria will be met.

The Company estimates forfeitures at the time of grant, and revises those estimates in subsequent periods if actual forfeitures differ from its estimates. The Company uses historical data to estimate forfeitures and records share-based compensation expense only for those awards that are expected to vest. To the extent that actual forfeitures differ from the Company’s estimates, the difference is recorded as a cumulative adjustment in the period the estimates were revised. For the years ended December 31, 2018, 2017 and 2016, the Company applied a forfeiture rate based on the Company’s historical forfeitures.

401(k) Plan

The Company maintains a defined contribution employee retirement plan (“401(k) plan”). For the years ended December 31, 2018, 2017 and 2016, the Company recognized expenses for matching contributions of $0.4 million, $0.3 million and $0.4 million, respectively.

Basic and Dilutive Net Loss Per Share of Common Stock

Basic net loss per share of common stock is computed by dividing net loss by the weighted-average number of shares of common stock outstanding during the period, excluding the dilutive effects of warrants to purchase common stock, non-vested restricted stock, stock options, and employee stock purchase plan purchase rights. Diluted net loss per share of common stock is computed by dividing net loss by the sum of the weighted-average number of shares of common stock outstanding during the period plus the potential dilutive effects of warrants to purchase common stock, non-vested restricted stock, stock options, and employee stock purchase plan purchase rights outstanding during the period calculated in accordance with the treasury stock method, but are excluded if their effect is anti-dilutive. Because the impact of these items is anti-dilutive during the periods of net loss, there was no difference between basic and diluted loss per share of common stock at December 31, 2018, 2017 and 2016.

Segments

The Company operates in only one segment. The chief operating decision-makers, who are the members of the Office of the Chief Executive Officer, and management use cash flows as the primary measure to manage the business and do not segment the business for internal reporting or decision making.

Impact of Recently Issued Accounting Standards

In February 2016, the FASB issued Accounting Standards Update (ASU) No. 2016-02, “Leases (Topic 842)”, and amended through subsequent ASUs, which increases transparency and comparability among companies accounting for lease transactions. The most significant change of this update will require the recognition of lease assets and liabilities on the balance sheet for lessees for operating lease arrangements with lease terms greater than 12 months. This ASU is effective for financial statements issued for annual periods and interim periods within those

annual periods, beginning after December 15, 2018. The Company adopted this standard effective January 1, 2019 using the alternative adoption method allowed by ASU 2018-11. The Company elected to use the package of three practical expedients which allows the Company not to reassess whether contracts are or contain leases, lease classification, and whether initial direct costs qualify for capitalization. The Company has substantially completed its assessment over the impact of the standard and determined that the only material leases that the Company holds are real estate operating lease commitments. Upon adoption of the standard, the Company preliminarily expects to record a right of use asset and lease liability of approximately $1.6 million on its consolidated balance sheets. The finalization of the Company's assessment may result in significant changes to its estimates that may materially impact its preliminary estimate of the cumulative effect.

Impact of Recently Adopted Accounting Standards

In May 2014, the FASB issued ASU No. 2014-09, “Revenue from Contracts with Customers (Topic 606).” The ASU establishes a principles-based approach for accounting for revenue arising from contracts with customers and supersedes existing revenue recognition guidance. The ASU provides that an entity should apply a five-step approach for recognizing revenue, including (1)

identify the contract with a customer; (2) identify the performance obligations in the contract; (3) determine the transaction price; (4) allocate the transaction price to the performance obligations in the contract; and (5) recognize revenue when, or as, the entity satisfies a performance obligation. Also, the entity must provide various disclosures concerning the nature, amount and timing of revenue and cash flows arising from contracts with customers. The FASB has issued several updates to the standard which (1) deferred the original effective date to annual periods and interim periods within those annual periods beginning after December 15, 2017, while allowing for early adoption as of January 1, 2017 (ASU 2015-14); (2) clarify the application of the principal versus agent guidance (ASU 2016-08); and (3) clarify the guidance on inconsequential and perfunctory promises and licensing (ASU 2016-10). The Company adopted ASU No. 2014-09 as of January 1, 2018 using the full retrospective approach and determined that there was no impact on its consolidated financial statements. In preparation for adoption of the standard, the Company implemented internal controls to enable the preparation of financial information, including the assessment of the impact of the standard.

In January 2016, the FASB issued ASU No. 2016-01, “Financial Instruments-Overall (Subtopic 825-10)-Recognition and Measurement of Financial Assets and Financial Liabilities.” The new standard enhances reporting for financial instruments. The ASU is effective for financial statements issued for annual periods and interim periods within those annual periods beginning after December 15, 2017. The Company adopted ASU No. 2016-01 on January 1, 2018 on a prospective basis. As a result of this standard, changes in fair value of available-for-sale equity securities that were previously recognized in other comprehensive income are now recognized in earnings. As of January 1, 2018, the Company had no unrealized gains or losses in other comprehensive income that had to be reclassified to retained earnings.

Note 2. Investments

The following tables summarize the Company's short-term and long-term debt investments (in thousands):

	December 31, 2018			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Corporate bonds	$32,724	$ —	$ (41)	$32,683
Commercial paper	60,159	—	(45)	60,114
U.S. Treasury securities	12,592	—	(3)	12,589
Total investments	$105,475	$ —	$ (89)	$105,386

	December 31, 2017			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
U.S. Treasury securities	$210,280	$ —	$ (963)	$209,317
Total investments	$210,280	$ —	$ (963)	$209,317

The following tables summarize the Company's debt investments with unrealized losses, aggregated by investment type and the length of time that individual investments have been in a continuous unrealized loss position (in thousands, except number of securities):

	December 31, 2018					
	Less than 12 Months		Greater than 12 Months		Total	
	Fair Value	Unrealized Loss	Fair Value	Unrealized Loss	Fair Value	Unrealized Loss

Corporate bonds	$32,683	$	(41	)	$ —	$ —	$32,683	$ (41)
Commercial paper	60,114		(45	)	— —		60,114	(45)
U.S. Treasury securities	12,589		(3	)	— —		12,589	(3)
Total	$105,386	$	(89	)	$ —	$ —	$105,386	$ (89)
Number of securities with unrealized losses			36			—		36

	December 31, 2017					
	Less than 12 Months		Greater than 12 Months		Total	
	Fair Value	Unrealized Loss	Fair Value	Unrealized Loss	Fair Value	Unrealized Loss
U.S. Treasury securities	$170,390	$ (871)	$38,927	$ (92)	$209,317	$ (963)
Total	$170,390	$ (871)	$38,927	$ (92)	$209,317	$ (963)
Number of securities with unrealized losses		39		7		46

The following table summarizes the scheduled maturity for the Company's debt investments at December 31, 2018 (in thousands):

	December 31, 2018
Maturing in one year or less	$ 105,386
Total debt investments	$ 105,386
Common stock of U.S. corporation	38
Total investments	$ 105,424

Note 3. Property and Equipment

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

	December 31,	
	2018	2017
Lab equipment	$2,599	$2,496
Leasehold improvements	1,550	1,552
Computer equipment	1,181	1,170
Office furniture and equipment	520	520
Property and equipment	5,850	5,738
Less accumulated depreciation	(4,640)	(3,844)
Property and equipment, net of accumulated depreciation	$1,210	$1,894

Note 4. Commitments and Contingencies

Leases

The Company leases its facilities and certain office equipment under long-term non-cancelable operating leases that expire at various dates through 2021. The Company has the following minimum rental payments under non-cancelable operating lease obligations that existed at December 31, 2018 (in thousands):

Years Ending December 31,	Minimum Rental Payment
2019	$ 786
2020	797
2021	235
Total future minimum rental payments	$ 1,818

Rent expense under non-cancelable operating leases and other month-to-month equipment rental agreements, including common area maintenance fees, totaled approximately $0.6 million, $0.5 million, and $0.7 million for the years ended December 31, 2018, 2017 and 2016, respectively.

81

Sublease

The Company subleases 3,537 square feet of its office space under a non-cancelable operating lease that expires February 2021. Total future minimum rentals under the non-cancelable operating sublease as of December 31, 2018 are presented below (in thousands):

Years Ending December 31,	Minimum Sublease Rentals
2019	$ 78
2020	81
2021	14
Total future minimum sublease rentals	$ 173

Significance of Revenue Source

The Company is the recipient of federal research contract funds from BARDA. Periodic audits are required under the grant and contract agreements and certain costs may be questioned as appropriate under the agreements. Management believes that such amounts in the current year, if any, are not significant. Accordingly, no provision for refundable amounts under the agreements has been made as of December 31, 2018 and 2017.

Note 5. Stockholders' Equity (Deficit)

Common Stock

The Company's common stock consists of 200 million authorized shares at December 31, 2018 and 2017, and 50.7 million and 47.5 million shares issued and outstanding at December 31, 2018 and December 31, 2017, respectively.

Shares Reserved for Future Issuance

The Company has reserved shares of common stock for future issuances as follows:

	December 31,	
	2018	2017
For exercise of common stock warrants	—	227,794
For exercise of outstanding common stock options	6,429,638	4,996,661
For delivery upon vesting of outstanding restricted stock units	656,169	956,299
For future equity awards under the 2013 Equity Incentive Plan	1,587,670	1,082,608
For future purchases under the 2013 Employee Stock Purchase Plan	2,120,290	1,861,472
Total shares of common stock reserved for future issuances	10,793,767	9,124,834

Stock Options

In connection with the Company's IPO, the Company adopted the 2013 Equity Incentive Plan (the 2013 Plan). The 2013 Plan provides for the grant of incentive stock options (ISOs), nonstatutory stock options (NSOs), stock appreciation rights, restricted stock awards, restricted stock unit (RSU) awards, performance-based stock awards, and other forms of equity compensation (collectively, stock awards), all of which may be granted to employees, including officers, non-employee directors and consultants of the Company and its affiliates. Additionally, the 2013 Plan provides for the grant of performance cash awards. ISOs may be granted only to employees. All other awards may be granted to employees, including officers, and to non-employee directors and consultants. The number of shares of

common stock reserved for issuance under the 2013 Plan will automatically increase on January 1 of each year, continuing through and including January 1, 2023, by 4.0% of the total number of shares of capital stock outstanding on December 31 of the preceding calendar year, or a lesser number of shares determined by the Company's board of directors.

The Company estimates the fair value of its share-based awards to employees, directors and consultants using the Black-Scholes option-pricing model. The Black-Scholes model requires the input of highly complex and subjective assumptions, including (a)

the expected stock price volatility, (b) the calculation of expected term of the award, (c) the risk-free interest rate and (d) expected dividends. Due to the Company's limited operating history and historical and implied volatility data, the Company has based its estimates of expected volatility on a blend of Company specific historical data and a group of similar public traded companies. When selecting these public companies on which it has based its expected stock price volatility, the Company selected companies with comparable characteristics to it, including enterprise value, risk profiles, positions within the industry, and with historical share price information sufficient to meet the expected life of its stock options. For employee stock options, the Company uses historical exercise data to estimate the expected life. The risk-free interest rates for the periods within the expected life of the option are based on the U.S. Treasury instrument with a life that is similar to the expected life of the option grant. The Company has never paid, and does not expect to pay, dividends in the foreseeable future.

The following table illustrates the assumptions for the Black-Scholes model used in determining the fair value of the stock options granted:

	Years Ended December 31,		
	2018	2017	2016
Expected volatility	85.83%	85.51%	85.16%
Expected term (in years)	5.9	5.9	6.0
Weighted-average risk-free interest rate	2.52%	2.02%	1.70%
Expected dividend yield	—%	—%	—%
Weighted-average fair value per option	$3.43	$3.71	$5.62

A summary of activity related to the Company's stock options is as follows:

	Number of Options Outstanding	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Life (in Years)	Total Intrinsic Value
Balance, December 31, 2016	4,342,466	$ 17.81	8.09	
Granted	928,816	5.17	—	
Exercised	(38,885)	3.98	—	
Forfeited	(235,736)	19.10	—	
Balance, December 31, 2017	4,996,661	$ 15.51	7.59	
Granted	2,050,995	4.73	—	
Exercised	(29,262)	3.93	—	
Forfeited	(588,756)	12.31	—	
Balance, December 31, 2018	6,429,638	$ 12.41	7.37	$39,873
Exercisable at December 31, 2018	4,119,234	$ 15.94	6.75	$39,873
Vested or expected to vest at December 31, 2018	6,366,085	$ 12.47	7.36	$39,873

As of December 31, 2018, there was approximately $8.7 million of total unrecognized compensation cost related to non-vested stock options granted under the 2013 Plan. That compensation cost is expected to be recognized over a weighted-average period of approximately 2.00 years years.

Other information regarding the Company's stock options is as follows (in thousands, except per share data):

	Years Ended December 31,		
	2018	2017	2016
Weighted-average grant-date fair value per share of options granted	$3.43	$3.71	$5.62
Total intrinsic value of options exercised	$31	$48	$119

Total fair value of shares vested	$11,021	$11,786	$13,330

The following table summarizes, at December 31, 2018, by price range: (1) for stock option awards outstanding under the 2013 Plan, the number of stock option awards outstanding, their weighted-average remaining life and their weighted-average exercise price; and (2) for stock option awards exercisable under the 2013 Plan, the number of stock option awards exercisable and their weighted-average exercise price:

	Outstanding			Exercisable	
Exercise Price Range ($)	Number	Weighted-Average Remaining Contractual Life (in years)	Weighted-Average Exercise Price	Number	Weighted-Average Exercise Price
1.57 to 7.57	3,139,495	8.37	$ 4.70	1,323,880	$ 4.54
7.58 to 8.06	1,696,746	7.02	8.06	1,239,595	8.06
8.07 to 18.75	261,805	5.07	18.59	261,805	18.59
18.76 to 39.17	559,663	5.55	25.32	556,525	25.25
39.18 to 53.74	771,929	6.22	41.90	737,429	41.71
1.57 to 53.74	6,429,638	7.37	$ 12.41	4,119,234	$ 15.94

Employee Stock Purchase Plan

In February 2013, the Company's board of directors adopted the 2013 Employee Stock Purchase Plan (ESPP), which was subsequently ratified by stockholders and became effective in April 2013. The purpose of the ESPP is to retain the services of new employees and secure the services of new and existing employees while providing incentives for such individuals to exert maximum efforts toward the Company's success and that of its affiliates. The ESPP initially authorized the issuance of 704,225 shares of common stock pursuant to purchase rights granted to the Company's employees or to employees of any of its designated affiliates. The number of shares of common stock reserved for issuance will automatically increase on January 1 of each calendar year, from January 1, 2014 through January 1, 2023 by the least of (a) 1% of the total number of shares of common stock outstanding on December 31 of the preceding calendar year, (b) 422,535 shares, or (c) a number determined by the Company's board of directors that is less than (a) and (b). The ESPP is intended to qualify as an "employee stock purchase plan" within the meaning of Section 423 of the Internal Revenue Code of 1986. The common stock reserved for future issuance under the ESPP was automatically increased by an additional 422,535 shares on January 1, 2017 and 2018, bringing the total number of shares of common stock that may be purchased under the ESPP to 2,226,261 and 2,648,796, respectively.

The Company has reserved a total of 2,648,796 shares of common stock to be purchased under the ESPP, of which 2,120,290 and 1,861,472 shares remained available for purchase at December 31, 2018 and 2017, respectively. Eligible employees may authorize an amount up to 15% of their salary to purchase common stock at the lower of a 15% discount to the beginning price of their offering period or a 15% discount to the ending price of each six-month purchase interval. The ESPP also provides for an automatic reset feature to start participants on a new twenty-four month participation period in the event that the common stock market value on a purchase date is less than the common stock value on the first day of the twenty-four month offering period. The Company issued 163,717 and 173,822 shares of common stock pursuant to the ESPP for the year ended December 31, 2018 and 2017, respectively. Compensation expense for purchase rights under the ESPP related to the purchase discount and the "look-back" option were determined using a Black-Scholes option pricing model.

The following table illustrates the assumptions for the Black-Scholes model used in determining the fair value of the ESPP purchase rights:

	Years Ended December 31,		
	2018	2017	2016
Expected volatility	44.01%	77.18%	111.57%
Expected term (in years)	1.23	0.97	1.37
Weighted-average risk-free interest rate	2.56%	0.99%	0.75%

Expected dividend yield	— %	— %	— %
Weighted-average option value per share	$1.36	$2.65	$3.20

As of December 31, 2018, the Company had a liability of $0.2 million representing employees' contributions to the ESPP.

Restricted Stock Units

For the years ended December 31, 2018 and 2017, the Company issued RSUs to certain employees which vest based on service criteria. When vested, the RSU represents the right to be issued the number of shares of the Company's common stock that is equal to the number of RSUs granted. The grant date fair value for RSUs is based upon the market price of the Company's common stock on the date of the grant. The fair value is then amortized to compensation expense over the requisite service period or vesting term. For the years ended December 31, 2018 and 2017, the Company issued 233,050 and 744,450 shares of common stock pursuant to the vesting of RSUs, respectively.

In January 2017, the Company also granted performance-based RSUs which, when vested, represent the right to be issued the number of shares of the Company's common stock that is equal to the number of RSUs granted. The grant date fair value for performance-based RSUs is based upon the market price of the Company's common stock on the date of the grant. For the portion of the performance-based RSUs of which the achievement of the performance condition is considered probable, the Company recognizes stock-based compensation expense on the related estimated fair value of such RSUs ratably for each vesting tranche from the service inception date to the end of the requisite service period. For the performance conditions that are not considered probable of achievement at the grant date or upon quarterly re-evaluation, prior to the event actually occurring, the Company begins recognizing the related stock-based compensation expense ratably when the event occurs or when the Company can determine that achievement of the performance condition is probable. In those cases, the Company recognizes the change in estimate at the time it determines the performance condition is probable of achievement (by recognizing stock-based compensation expense as cumulative catch-up adjustment as if the Company had estimated at the grant date that the performance condition would have been achieved) and recognize the remaining compensation cost through the end of the requisite service period. The Company issued no shares of common stock pursuant to the vesting of performance-based RSUs for the year ended December 31, 2018 and 2017.

A summary of activity related to the Company’s RSUs is as follows:

	Number of Restricted Stock Units Outstanding	Weighted-Average Grant-Date Fair Value
Balance, December 31, 2017	956,299	$ 5.08
Granted	153,375	4.42
Share issuance	(233,050)	5.05
Forfeited	(220,455)	5.12
Balance, December 31, 2018	656,169	$ 4.92

The total unrecognized compensation cost related to the non-vested RSUs as of December 31, 2018 was $3.9 million and will be recognized over a weighted average period of approximately 2.14 years years.

Warrants

In February 2011, the Company issued warrants to purchase an aggregate of 5,501,215 shares of Series F redeemable convertible preferred stock at an exercise price of $2.045 per share. Upon the completion of the Company’s IPO in April 2013, these warrants were converted into warrants to purchase 1,549,628 shares of common stock at an exercise price of $7.26 per share. At December 31, 2017, warrants for the purchase of 227,794 shares of common stock were issued, outstanding and exercisable. The warrants were exercisable at any time and expired on February 7, 2018.

85

Stock-based Compensation

For awards with only service conditions and graded-vesting features, the Company recognizes compensation expense on a straight-line basis over the requisite service period. Total stock-based compensation expense was as follows (in thousands):

	Years Ended December 31,		
	2018	2017	2016
Income Statement Classification:			
Research and development expense	$5,343	$7,047	$7,137
General and administrative expense	7,731	9,063	9,086
Total stock-based compensation expense	$13,074	$16,110	$16,223

Cash received from exercises under all share-based payment arrangements for 2018, 2017 and 2016 was $0.7 million, $0.8 million and $0.6 million, respectively. There was no actual tax benefit realized for the tax deductions from exercises of the share-based payment arrangements during 2018, 2017 or 2016.

At-The-Market Equity Offering

On November 8, 2017, the Company entered into an at-the-market (ATM) sales agreement with Cowen and Company, LLC to sell up to $75 million of the Company's common stock under a shelf registration statement filed in November 2017. During the year ended December 31, 2018, the Company sold 2.8 million shares of common stock at a weighted average price per share of $4.00 for $10.9 million of proceeds net of commissions.

Note 6. Income Taxes

No income tax expense or benefit has been recorded for the years ended December 31, 2018, 2017 or 2016. This is due to the establishment of a valuation allowance against the deferred tax assets generated during those periods. At December 31, 2018, the Company has concluded that it is more likely than not that the Company may not realize the benefit of its deferred tax assets due to its history of losses. Accordingly, the net deferred tax assets have been fully reserved.

A reconciliation of the difference between the benefit for income taxes and income taxes at the statutory U.S. federal income tax rate is as follows for the years ended December 31, 2018, 2017, and 2016 (in thousands, except percentages):

	2018		2017		2016	
	Amount	% of Pretax Earnings	Amount	% of Pretax Earnings	Amount	% of Pretax Earnings
Income tax benefit at statutory rate	$(14,590)	21.0 %	$(24,134)	34.0 %	$(25,973)	34.0 %
State income taxes	(792)	1.1 %	(1,090)	1.5 %	(1,544)	2.0 %
Research and development credits	(1,798)	2.6 %	(2,039)	2.9 %	(2,691)	3.5 %
Foreign rate differential	2	— %	60	(0.1)%	(2)	— %
Permanent items	1,164	(1.7)%	1,646	(2.3)%	2,537	(3.3)%
Provision to return adjustments	621	(0.9)%	1,212	(1.7)%	259	(0.3)%
Effect of change in federal tax rate	—	— %	57,950	(81.6)%	—	— %
Effect of change in state tax rate	151	(0.2)%	193	(0.3)%	1,585	(2.1)%
Removal of excess tax benefit	—	— %	(12,930)	18.2 %	—	— %
Increase in unrecognized tax benefits	450	(0.7)%	403	(0.6)%	444	(0.6)%

Change in valuation allowance	14,792	(21.2)%	(21,271)	30.0 %	25,385	(33.2)%
Net benefit	$—	— %	$—	— %	$—	— %

The components of deferred tax assets and liabilities at December 31, 2018 and 2017 were as follows (in thousands):

	December 31,	
	2018	2017
Deferred tax assets:		
Domestic net operating loss carryforwards	$104,708	$92,020
Foreign net operating loss carryforwards	71	61
Research and development expenses	1,002	763
Capitalized Section 174 expenses	25	28
Research and development credits	13,789	12,437
Accrued bonuses	500	777
Share-based compensation	7,144	6,156
Other	778	983
Total gross deferred tax assets	128,017	113,225
Valuation allowance	(128,017)	(113,225)
Total deferred tax assets	—	—
Deferred tax liabilities:		
Other	—	—
Total deferred tax liabilities	—	—
Total deferred tax assets and liabilities, net	$—	$—

At December 31, 2018, the Company had net operating loss carryforwards for federal, state, and foreign tax purposes of approximately $465.3 million, $353.8 million and $0.4 million, respectively. At December 31, 2017, the Company had net operating loss carryforwards for federal, state, and foreign tax purposes of approximately $408.1 million, $319.9 million and $0.4 million, respectively. Federal losses of $408.1 million begin to expire in 2020 and $57.2 million of the federal losses carryforward indefinitely. The state losses begin to expire in 2019. The foreign losses do not expire. In addition, the Company has tax credit carryforwards for federal tax purposes of approximately $18.4 million as of December 31, 2018, which begin to expire in 2022. The future utilization of net operating loss and tax credit carryforwards may be limited due to changes in ownership. Management has recorded a valuation allowance for all of the deferred tax assets due to the uncertainty of future taxable income.

The Company incorporated a subsidiary in the United Kingdom in 2014. However, the subsidiary has had minimal activity since inception. The subsidiary has primarily recorded net losses since inception and recorded a net loss as of December 31, 2018 and as such, has no undistributed earnings.

The Company incorporated a subsidiary in Ireland during 2018. However, the subsidiary had minimal activity during the year and as such, has no undistributed earnings.

In general, if the Company experiences a greater than 50% aggregate change in ownership of certain significant stockholders over a three-year period (a Section 382 ownership change), utilization of its pre-change net operating loss carryforwards is subject to an annual limitation under Section 382 of the Internal Revenue Code of 1986, as amended (and similar state laws). The annual limitation generally is determined by multiplying the value of the Company’s stock at the time of such ownership change (subject to certain adjustments) by the applicable long-term tax-exempt rate. Such limitations may result in expiration of a portion of the net operating loss carryforwards before utilization and may be substantial. The ability of the Company to use its net operating loss carryforwards may be limited or lost if the Company experiences a Section 382 ownership change in connection with offerings or as a result of future changes in its stock ownership. Losses from a specific period may be subject to multiple limitations, and would generally be limited by the lowest of those limitations.

The Company has determined that a Section 382 ownership change occurred in 2002, and as such, losses incurred prior to that date are subject to an annual limitation of at least $64,000. Additionally, the Company has determined that a Section 382 ownership change occurred in 2007, and as such, losses incurred prior to that date are subject to an annual limitation of at least $762,000. The Company evaluated Section 382 ownership changes subsequent to 2007 through September 30, 2018 and concluded that a Section 382 ownership change occurred in 2013 as a result of the initial public offering. As such, losses incurred prior to that date are subject to an annual limitation of at least $6.7 million.

As of December 31, 2017, the Company has adopted ASU 2016-09 which is effective for public companies for annual periods beginning after December 15, 2016. The ASU requires all excess tax benefits and tax deficiencies to be recognized as income tax expense or benefit in the income statement in the year in which they occur. As such, the Company has grossed up its net operating loss deferred tax asset to include all excess tax benefits as of December 31, 2017.

The Company has determined that there may be a future limitation on the Company's ability to utilize its entire federal R&D credit carryover. Therefore, the Company recognized an uncertain tax benefit associated with the federal R&D credit carryover during the years ended December 31, 2018 and 2017, as follows (in thousands):

Balance at December 31, 2016	$2,400
Increases related to 2017	403
Increases related to prior periods	473
Balance at December 31, 2017	3,276
Increases related to 2018	450
Increases related to prior periods	—
Balance at December 31, 2018	$3,726

The change in the amount of the unrecognized tax benefits accrued for prior years is due to the change in the federal tax rate and is reflected as a component of such in the statutory rate reconciliation.

The Company has determined that it had no other material uncertain tax benefits for the year ended December 31, 2018. As of January 1, 2019, due to the carry forward of unutilized net operating losses and research and development credits, the Company is subject to U.S. federal and state income tax examinations for the tax years 2000 through 2018. The Company recognizes accrued interest related to unrecognized tax benefits in interest expense and penalties in operating expense. No amounts were accrued for the payment of interest and penalties at December 31, 2018.

On December 22, 2017, the Tax Act was enacted into law, which reduced the federal corporate income tax rate to 21% for tax years beginning after December 31, 2017. As a result of the revised tax rate, the Company adjusted its deferred tax assets as of December 31, 2017 by applying the revised 21% rate, which resulted in a decrease to the deferred tax assets and a corresponding decrease to the valuation allowance of approximately $58 million.

The Tax Act also implements a territorial tax system. Under the territorial tax system, in general, the Company's foreign earnings will no longer be subject to tax in the U.S. As part of the transition to the territorial tax system the Tax Act included a mandatory deemed repatriation of all undistributed foreign earnings that are subject to a U.S. income tax. The Company has determined that the deemed repatriation applicable to the year ended December 31, 2017 does not result in an additional U.S. income tax liability as it has no undistributed foreign earnings.

The Tax Act subjects a US shareholder to tax on global intangible low-taxed income (GILTI) earned by certain foreign subsidiaries. The FASB Staff Q&A, Topic 740, No. 5, Accounting for Global Intangible Low-Taxed Income, states that an entity can make an accounting policy election to either recognized deferred taxes for temporary basis differences expected to reverse as GILTI in future years or to provide for the tax expense related to GILTI in the year the tax is incurred as a period expense only. Because the Company was evaluating the provision of GILTI as of December 31, 2017, no GILTI-related deferred amounts were recorded in 2017. The Company has elected to account for GILTI in the year the tax is incurred. The Company does not have a GILTI inclusion in 2018; therefore, no GILTI tax has been recorded for the year ended December 31, 2018.

The SEC staff issued Staff Accounting Bulletin No. 118, Income Tax Accounting Implications of the Tax Cuts and Jobs Act (SAB 118) which allows the Company to record provisional amounts during a measurement period which is similar to the measurement period used when accounting for business combinations. At December 31, 2017

provisional amounts were recorded related to deferred taxes for stock compensation and the deferred rate change. At December 31, 2018 the measurement period has ended and the Company's accounting related to the Tax Act is complete. The Company did not make any measurement-period adjustments related to the provisional items recorded as of December 31, 2017.

Note 7. Significant Agreements

The Regents of the University of California

In May 2002, the Company entered into a license agreement with The Regents of the University of California (UC) under which the Company obtained an exclusive, worldwide license to UC’s patent rights in certain inventions (the UC Patent Rights) related

to lipid-conjugated antiviral compounds and their use, including certain patents relating to brincidofovir. The license agreement was amended in September 2002 in order to expand the scope of the license and again in December 2010 in order to modify certain financial terms. The agreement was amended a third time in September 2011 to add additional patents related to certain metabolically stable lipid-conjugate compounds. A fourth amendment was executed in July 2012 to alter the rights and obligations of the parties in light of the Company's current business plans. In April 2018, a fifth amendment was executed to alter the rights and obligations of the parties in light of the Company's current business plans and to extend the term of the agreement to the later of the longest-lived Patent Rights (as defined in the agreement) or May 2028.

Under the license agreement, the Company is permitted to research, develop, manufacture and commercialize products utilizing the UC Patent Rights for all human and veterinary uses, and to sublicense such rights. UC retained the right, on behalf of itself and other non-profit institutions, to use the UC Patent Rights for educational and research purposes and to publish information about the UC Patent Rights.

In consideration for the rights granted under the license agreement, the Company has issued UC an aggregate of 64,788 shares of common stock. As additional consideration, the Company is required to pay certain cash milestone payments in connection with the development and commercialization of compounds that are covered by the UC Patent Rights, plus certain annual fees to maintain such patents until the Company commercializes a product utilizing UC Patent Rights. In connection with the development and commercialization of brincidofovir and CMX157, the Company could be required to pay UC up to an aggregate of $3.4 million in milestone payments, assuming the achievement of all applicable milestone events under the license agreement. In addition, upon commercialization of any product utilizing the UC Patent Rights (which would include the commercialization of brincidofovir), the Company will be required to pay low single digit royalties on net sales of such product.

The license agreement requires that we diligently develop, manufacture and commercialize compounds that are covered by the UC Patent Rights, and we have agreed to meet certain development and commercialization milestones. UC may, at its option, either terminate the license agreement or change the license granted from an exclusive license to a non-exclusive license if we fail to meet such development and commercialization milestones. We are currently in compliance with these milestone requirements.

In the event the Company sublicenses a UC Patent Right (including UC Patent Rights relating to brincidofovir or CMX157) the Company is obligated to pay to UC a fee, which amount will vary depending upon the amount of any payments the Company receives and the clinical development stage of the compound being sublicensed, but which could be up to approximately 50% of the sublicense fee in certain circumstances. With respect to brincidofovir, the fee payable to UC will not exceed 5% of the sublicense fee. In addition, the Company will also be required to pay to UC a low single digit sublicense royalty on net sales of products that use the sublicensed UC Patent Rights, but in no event will the Company be required to pay more than 50% of the royalties it receives in connection with the relevant sublicense. Any such royalty payment will be reduced by other payments the Company is required to make to third parties until a minimum royalty has been reached.

Biomedical Advanced Research and Development Authority (BARDA)

In February 2011, the Company entered into a contract with BARDA for the advanced development of brincidofovir as a medical countermeasure in the event of a smallpox release. Under the contract, BARDA will reimburse the Company, plus pay a fixed fee, for the research and development of brincidofovir as a broad-spectrum therapeutic antiviral for the treatment of smallpox infections. The contract consists of an initial performance period, referred to as the base performance segment, plus up to four extension periods, referred to as option segments, each of which may be exercised at BARDA's sole discretion. The Company must complete the agreed upon milestones and deliverables in each discrete work segment before the next option segment is eligible to be exercised. Under the contract as currently

in effect, the Company may receive up to $75.8 million in expense reimbursement and $5.3 million in fees.

The Company is currently performing under the second and third option segments of the contract during which the Company may receive up to a total of $23.9 million and $14.1 million in expense reimbursement and fees, respectively. The second option segment is scheduled to end on August 1, 2019 and the third option segments is scheduled to end on March 30, 2019. Of the $75.8 million in expense reimbursement and $5.3 million in fees that the Company may receive, approximately $74.3 million in expense reimbursement and fees has been funded. As of December 31, 2018, of the total funding the Company had invoiced an aggregate of $62.6 million with respect to the base performance segment and the first three extension periods. For the years ended December 31, 2018, 2017, and 2016, the Company recognized revenue under this contract of $7.2 million, $4.5 million and $5.7 million, respectively.

ContraVir Pharmaceuticals

On December 17, 2014, the Company entered into a license agreement with ContraVir Pharmaceuticals (Nasdaq: CTRV) for the development and commercialization of CMX157 for certain antiviral indications. Under the terms of the agreement, ContraVir has sole responsibility with respect to the control of the development and commercialization of CMX157.

In exchange for the license to CMX157 rights, the Company received an upfront payment consisting of ContraVir Series B Convertible Preferred Stock which the Company converted into shares of ContraVir common stock in 2016. As of December 31, 2018 and 2017, the fair value of the investment was recorded as a short-term investment of $38 thousand and $0.4 million, respectively.

In addition, the Company is eligible to receive up to approximately $20 million in clinical, regulatory and initial commercial milestones in the United States and Europe, as well as royalties and additional milestones based on commercial sales in those territories. Either party may terminate the license agreement upon the occurrence of a material breach by the other party (subject to standard cure periods), or upon certain events involving the bankruptcy or insolvency of the other party. ContraVir may also terminate the license agreement without cause on a country-by-country basis upon sixty days' prior written notice.

University of Michigan

In 2006, the Company entered into a license agreement with The Regents of the University of Michigan (UM) under which the Company obtained an exclusive, worldwide license to UM's patent rights in certain inventions (UM Patent Rights) related to certain compounds originally synthesized at UM. Under the license agreement, the Company is permitted to research, develop, manufacture and commercialize products utilizing the UM Patent Rights, and to sublicense such rights subject to certain sublicensing fees and royalty payments.

In consideration for the rights granted to the Company, under the license agreement as amended in December 2016, the Company paid UM $50,000 in fees in 2016 and in January 2017 issued UM an aggregate of 33,058 shares of its common stock. In connection with the Company's commercialization or sublicensing of certain products covered by the license agreement, including CMX521, the Company could be required to pay royalties on net sales of such products ranging from 0.25% to 2%. Beginning in 2024, the Company is also subject to certain minimum annual royalty payments.

The UM license agreement requires that the Company uses commercially reasonable efforts to develop and make commercially available licensed products as soon as practicable. Specifically, the Company has agreed to make the first commercial sale of a licensed product by June of 2026. UM may terminate the license agreement if the Company materially breaches the license agreement. The Company is currently in compliance with its milestone requirements.

Note 8. Selected Quarterly Financial Data (Unaudited)

The following financial information reflects all normal recurring adjustments, which are, in the opinion of management, necessary for a fair statement of the results of the interim periods. Summarized quarterly data for 2018 and 2017 are as follows (in thousands, except share and per share data):

	2018 Quarters			
	Fourth	Third	Second	First
Revenue	$4,864	$ 369	$ 1,193	$ 790
Operating loss	(15,419)	(16,710)	(19,169)	(20,307)
Net loss	(14,956)	(16,079)	(18,613)	(19,826)
Net loss per share, basic and diluted	$(0.29)	$ (0.33)	$ (0.39)	$ (0.42)
Weighted-average shares outstanding, basic and diluted	50,722,658	48,172,354	47,811,552	47,637,907

	2017 Quarters			
	Fourth	Third	Second	First
Revenue	$1,844	$ 897	$ 675	$ 1,078
Operating loss	(18,687)	(17,910)	(17,245)	(18,260)
Net loss	(19,238)	(17,312)	(16,680)	(17,754)
Net loss per share, basic and diluted	$(0.41)	$ (0.37)	$ (0.36)	$ (0.38)
Weighted-average shares outstanding, basic and diluted	47,341,274	47,065,756	46,863,753	46,573,394

Net loss per share is computed independently for each of the quarters presented. Therefore, the sum of the quarterly per share calculations will not necessarily equal the annual per share calculation. Diluted weighted-average shares outstanding are identical to basic weighted-average shares outstanding and diluted net loss per share is identical to basic net loss per share for all quarters of 2018 and 2017.

Note 9. Subsequent Events

The Company has evaluated subsequent events through the issuance date of these financial statements to ensure that this filing includes appropriate disclosure of events both recognized in the financial statements as of December 31, 2018, and events which occurred subsequently but were not recognized in the financial statements.

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 principal executive officer and principal financial officer, after evaluating the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) of the Securities Exchange Act of 1934, as amended, or Exchange Act) as of December 31, 2018, have concluded that, based on such evaluation, our disclosure controls and procedures were effective to ensure that information required to be disclosed by us in the reports we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC, and is accumulated and communicated to our management, including our principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure.

Management’s Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Exchange Act Rules 13a-15(f) and 15d-15(f). Our internal control system was designed to provide reasonable assurance to our management and Board of Directors regarding the preparation and fair presentation of published financial statements.

Our internal control over financial reporting includes those policies and procedures that:

i. pertain to the maintenance of records, that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of our assets;

ii. provide reasonable assurance that transactions are recorded as necessary to permit preparations of financial statements in accordance with generally accepted accounting principles, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors; and

iii. provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on the financial statements.

All internal control systems, no matter how well designed, have inherent limitations. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation. In making the assessment of internal controls over financial reporting, our management used the criteria issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control-Integrated Framework (2013 framework). Based on that assessment and those criteria, management has concluded that our internal control over financial reporting was effective as of December 31, 2018.

Ernst & Young LLP, the independent registered public accounting firm that audited our financial statements included in this Annual Report, has issued an attestation report on the Company's internal control over financial reporting, a copy of which appears in Item 8 of this Annual Report.

Changes in Internal Control Over Financial Reporting

No change in our internal control over financial reporting (as defined in Rules 13a-15(d) and 15d-15(d) under the Exchange Act) occurred during the last fiscal quarter that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

Not applicable.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required by this item and not set forth below will be set forth in the section headed “Election of Directors” and “Executive Officers” in our Proxy Statement for our 2019 Annual Meeting of Stockholders (Proxy Statement), to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2018, and is incorporated herein by reference.

We have adopted a code of ethics for directors, officers (including our principal executive officer, principal financial officer and principal accounting officer) and employees, known as the Code of Business Conduct and Ethics. The Code of Business Conduct and Ethics is available on our website at http://www.chimerix.com under the Corporate Governance section of our Investor Relations page. We will promptly disclose on our website (i) the nature of any amendment to the policy that applies to our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions and (ii) the nature of any waiver, including an implicit waiver, from a provision of the policy that is granted to one of these specified individuals that is required to be disclosed pursuant to SEC rules and regulations, the name of such person who is granted the waiver and the date of the waiver.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this item will be set forth in the section headed “Executive Compensation” in our Proxy Statement 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 will be set forth in the section headed “Security Ownership of Certain Beneficial Owners and Management” in our Proxy Statement and is incorporated herein by reference.

The information required by Item 201(d) of Regulation S-K will be set forth in the section headed “Executive Compensation” in our Proxy Statement and is incorporated herein by reference.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required by this item will be set forth in the section headed “Transactions With Related Persons” in our Proxy Statement and is incorporated herein by reference.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

The information required by this item will be set forth in the section headed “Ratification of Selection of Independent Registered Public Accounting Firm” in our Proxy Statement and is incorporated herein by reference.

PART IV

ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES

1. Financial Statements. The financial statements and reports of independent registered public accounting firm are filed as part of this Annual Report (see "Index to Consolidated Financial Statements" at Item 8).

2. Financial Statement Schedules. No financial statement schedules are included because the information is either provided in the consolidated financial statements, is not required under the instructions or is immaterial, and such schedules, therefore have been omitted.

3. Exhibits. The following exhibits have been or are being filed herewith and are numbered in accordance with Item 601 of Regulation S-K:

EXHIBIT INDEX

Exhibit Number	Description of Document
3.1 (1)	Amended and Restated Certificate of Incorporation of the Registrant.
3.2 (1)	Amended and Restated Bylaws of the Registrant.
4.1 (1)	Form of Common Stock Certificate of the Registrant.
10.1+ (1)	Form of Indemnity Agreement by and between the Registrant and its directors and officers.
10.2+ (1)	Chimerix, Inc. 2002 Equity Incentive Plan and Form of Stock Option Agreement, Notice of Exercise and Form of Stock Option Grant Notice thereunder.
10.3+ (1)	Chimerix, Inc. 2012 Equity Incentive Plan and Form of Stock Option Agreement, Notice of Exercise and Form of Stock Option Grant Notice and Form of Restricted Stock Unit Award Agreement and Form of Restricted Stock Unit Award Grant Notice thereunder.
10.4+(17)	Form of Stock Option Agreement, Notice of Exercise and Form of Stock Option Grant Notice and Form of Restricted Stock Unit Award Agreement and Form of Restricted Stock Unit Award Grant Notice under Chimerix, Inc. 2013 Equity Incentive Plan.
10.5+ (2)	Chimerix, Inc. 2013 Equity Incentive Plan, as amended.
10.6+ (1)	Chimerix, Inc. 2013 Employee Stock Purchase Plan.
10.7+(25)	Chimerix, Inc. Non-Employee Director Compensation Policy.
10.8+ (26)	Chimerix, Inc. Officer Severance Benefit Plan, as amended.
10.9+ (1)	Employment Offer Letter to Timothy W. Trost dated March 16, 2011.
10.10+ (1)	Employment Offer Letter to M. Michelle Berrey, M.D., M.P.H. dated November 7, 2012.
10.11+ (3)	Employment Offer Letter to William Garrett Nichols, M.D., M.S., dated August 19, 2014.
10.12+ (12)	Directorship Offer Letter to James M. Daly dated June 6, 2014.
10.13+ (12)	Directorship Offer Letter to Catherine L. Gilliss dated June 13, 2014.
10.14+ (12)	Directorship Offer Letter to Patrick Machado dated May 30, 2014.
10.15+ (12)	Directorship Offer Letter to Ronald C. Renaud, Jr. dated December 12, 2014.
10.16 (1)	Office Lease by and between the Registrant and ACP 2505 Meridian LLC dated September 1, 2007, as amended.
10.17 (6)	Lease Agreement by and between the Registrant and Northwood RTC LLC dated March 10, 2014.
10.18 (5)	Fifth Amendment to Office Lease dated July 2, 2014 by and between the Registrant and AREP Meridian I LLC.
10.19 (9)	

	Sixth Amendment to Office Lease dated April 28, 2015 by and between the Registrant and IVC Meridian TT O, LLC.
10.20 (17)	Seventh Amendment to Office Lease dated March 10, 2017 by and between the Registrant and IVC Meridian TT O, LLC.
10.21 (18)	Eighth Amendment to Office Lease dated July 13, 2017 by and between the Registrant and IVC Meridian TT O, LLC.
10.22* (1)	Contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.

10.23* [7]	Contract modification No. 14, dated May 30, 2013, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.24* [8]	Contract modification No. 15, dated August 28, 2013, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.25* [8]	Contract modification No. 16, dated December 10, 2013, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.26 [4]	Contract modification No. 17, dated April 14, 2014, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.27 [12]	Contract modification No. 18, dated May 6, 2014, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.28* [5]	Contract modification No. 19, dated August 27, 2014, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.29 [5]	Contract modification No. 20, dated October 27, 2014, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.30* [12]	Contract modification No. 21, dated November 7, 2014, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.31 [12]	Contract modification No. 22, dated December 11, 2014, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.32 [12]	Contract modification No. 23, dated December 22, 2014, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.33 [12]	Contract modification No. 24, dated February 19, 2015, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.34 [9]	Contract modification No. 25, dated March 26, 2015, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.35 [10]	Contract modification No. 26, dated June 18, 2015, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.36 [10]	Contract modification No. 27, dated July 14, 2015, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.37* [11]	Contract modification No. 28, dated September 1, 2015, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.38* [11]	Contract modification No. 29, dated September 11, 2015, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.39* [13]	

	Contract modification No. 30, dated November 12, 2015, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.40* (14)	Contract modification No. 31, dated April 8, 2016, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.41* (14)	Contract modification No. 32, dated May 5, 2016, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.42* (15)	Contract modification No. 33, dated June 17, 2016, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.

10.43* (16)	Contract modification No. 34, dated August 3, 2016, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.44 (17)	Contract modification No. 35, dated October 21, 2016, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.45 (17)	Contract modification No. 36, dated January 23, 2017, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.46 (18)	Contract modification No. 37, dated March 27, 2017, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.47 (19)	Contract modification No. 38, dated April 3, 2017, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.48 (19)	Contract modification No. 39, dated May 11, 2017, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.49 (19)	Contract modification No. 40, dated June 16, 2017, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.50 (20)	Contract modification No. 41, dated July 24, 2017, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.51 (20)	Contract modification No. 42, dated August 25, 2017, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.52 (20)	Contract modification No. 43, dated September 22, 2017, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.53 (20)	Contract modification No. 44, dated September 28, 2017, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.54(22)	Contract modification No. 45, dated October 20, 2017, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.55(22)	Contract modification No. 46, dated November 27, 2017, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.56*(22)	Contract modification No. 47, dated December 21, 2017, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.57(22)	Contract modification No. 48, dated December 21, 2017, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.58*(22)	Contract modification No. 49, dated February 27, 2018, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.59*(23)	

Contract modification No. 50, dated March 20, 2018, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.

10.60*[24]	Contract modification No. 51, dated May 31, 2018, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.61*[24]	Contract modification No. 52, dated July 11, 2018, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.62[25]	Contract modification No. 53, dated September 6, 2018, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.63	Contract modification No. 54, dated December 3, 2018, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.64**	Contract modification No. 55, dated January 10, 2019, to the contract by and between the Registrant and the Biomedical Advanced Research and Development Authority of the United States Department of Health and Human Services dated February 16, 2011, as amended.
10.65*[17]	Patent Option and License Agreement by and between the Registrant and The Regents of the University of Michigan dated May 24, 2006, as amended.
10.66*[1]	License Agreement by and between the Registrant and The Regents of the University of California dated May 13, 2002, as amended.
10.67[21]	Sales Agreement, dated November 8, 2017, by and between Chimerix, Inc and Cowen and Company, LLC.
10.68[22]	First Amendment to Industrial Building Lease dated December 14, 2017 by and between Registrant and CLPF - Research Center, LLC.
10.69[23]	Fifth Amendment, dated April 24, 2018, to the License Agreement by and between the Registrant and The Regents of the University of California dated May 13, 2002, as amended.
10.70+	Agreement and Release, dated February 8, 2019, by and between the Registrant and M. Michelle Berrey.
10.71+	Employment Offer Letter to Michael A. Alrutz dated May 9, 2012.
23.1	Consent of Ernst & Young LLP, an Independent Registered Public Accounting Firm.
24.1	Power of Attorney. Reference is made to the signature page hereto.
31.1	Certification of Principal Executive Officer, pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2	Certification of Principal Financial Officer, pursuant to Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1	Certification of Principal Executive Officer, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2	Certification of Principal Financial Officer, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS	XBRL Instance Document.
101.SCH	XBRL Taxonomy Extension Schema Document.
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document.
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document.
101.LAB	XBRL Taxonomy Extension Label Linkbase Document.
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document.

+ Indicates management contract or compensatory plan.

* Confidential treatment has been granted with respect to certain portions of this exhibit. Omitted portions have been filed separately with the SEC.

** Confidential treatment has been requested with respect to certain portions of this exhibit. Omitted portions have been filed separately with the SEC.

(1) Incorporated by reference to Chimerix, Inc.'s Registration Statement on Form S-1 (No. 333-187145), as amended.

(2) Incorporated by reference to Chimerix, Inc.'s Current Report on Form 8-K (No. 001-35867) filed with the SEC on June 23, 2014.

(3) Incorporated by reference to Chimerix, Inc.'s Current Report on Form 8-K (No. 001-35867) filed with the SEC on September 4, 2014.

(4) Incorporated by reference to Chimerix, Inc.'s Quarterly Report on Form 10-Q (No. 001-35867) filed with the SEC on May 9, 2014.

(5) Incorporated by reference to Chimerix, Inc.'s Quarterly Report on Form 10-Q (No. 001-35867) filed with the SEC on November 7, 2014.

(6) Incorporated by reference to Chimerix, Inc.'s Current Report on Form 8-K (No. 001-35867) filed with the SEC on March 14, 2014.

(7) Incorporated by reference to Chimerix, Inc.'s Quarterly Report on Form 10-Q (No. 001-35867) filed with the SEC on August 14, 2013.

(8) Incorporated by reference to Chimerix, Inc.'s Annual Report on Form 10-K (No. 001-35867) filed with the SEC on March 7, 2014.

(9) Incorporated by reference to Chimerix, Inc.'s Quarterly Report on Form 10-Q (No. 001-35867) filed with the SEC on May 11, 2015.

(10) Incorporated by reference to Chimerix, Inc.'s Quarterly Report on Form 10-Q (No. 001-35867) filed with the SEC on August 6, 2015.

(11) Incorporated by reference to Chimerix, Inc.'s Quarterly Report on Form 10-Q (No. 001-35867) filed with the SEC on November 5, 2015.

(12) Incorporated by reference to Chimerix, Inc.'s Annual Report on Form 10-K (No. 001-35867) filed with the SEC on March 6, 2015.

(13) Incorporated by reference to Chimerix, Inc.'s Annual Report on Form 10-K (No. 001-35867) filed with the SEC on February 29, 2016

(14) Incorporated by reference to Chimerix, Inc.'s Quarterly Report on Form 10-Q (No. 001-35867) filed with the SEC on May 9, 2016.

(15) Incorporated by reference to Chimerix, Inc.'s Quarterly Report on Form 10-Q (No. 001-35867) filed with the SEC on August 8, 2016.

(16) Incorporated by reference to Chimerix, Inc.'s Quarterly Report on Form 10-Q (No. 001-35867) filed with the SEC on November 7, 2016.

(17) Incorporated by reference to Chimerix, Inc.'s Annual Report on Form 10-K (No. 001-35867) filed with the SEC on March 2, 2017.

(18) Incorporated by reference to Chimerix, Inc.'s Quarterly Report on Form 10-Q (No. 001-35867) filed with the SEC on May 9, 2017.

(19) Incorporated by reference to Chimerix, Inc.'s Quarterly Report on Form 10-Q (No. 001-35867) filed with the SEC on August 7, 2017.

(20) Incorporated by reference to Chimerix, Inc.'s Current Report on Form 8-K (No. 001-35867) filed with the SEC on October 11, 2017.

(21) Incorporated by reference to Chimerix, Inc.'s Current Report on Form 8-K (No. 001-35867) filed with the SEC on November 8, 2017.

(22) Incorporated by reference to Chimerix, Inc.'s Annual Report on Form 10-K (No. 001-35867) filed with the SEC on March 1, 2018.

(23) Incorporated by reference to Chimerix, Inc.'s Quarterly Report on Form 10-Q (No. 001-35867) filed with the SEC on May 7, 2018.

(24) Incorporated by reference to Chimerix, Inc.'s Quarterly Report on Form 10-Q (No. 001-35867) filed with the SEC on August 8, 2018.

(25) Incorporated by reference to Chimerix, Inc.'s Quarterly Report on Form 10-Q (No. 001-35867) filed with the SEC on November 8, 2018.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this Annual Report on Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized.

Chimerix, Inc.

Date: March 5, 2019 By: /s/ Michael A. Alrutz
Michael A. Alrutz
Principal Executive Officer

POWER OF ATTORNEY

KNOW ALL MEN BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Michael A. Alrutz and Timothy W. Trost, and each of them, his true and lawful attorneys-in-fact, each with full power of substitution, for him in any and all capacities, to sign any amendments to this Annual Report on Form 10-K and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, hereby ratifying and confirming all that each of said attorneys-in-fact or their substitute or substitutes may do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this Annual Report on Form 10-K has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Michael A. Alrutz Michael A. Alrutz	Principal Executive Officer	March 5, 2019
/s/ Timothy W. Trost Timothy W. Trost	Principal Financial and Accounting Officer	March 5, 2019
/s/ Martha J. Demski Martha J. Demski	Chair of the Board of Directors	March 5, 2019
/s/ James M. Daly James M. Daly	Member of the Board of Directors	March 5, 2019
/s/ Catherine L. Gilliss Catherine L. Gilliss, PhD, RN, FAAN	Member of the Board of Directors	March 5, 2019
/s/ Edward F. Greissing Jr. Edward F. Greissing Jr.	Member of the Board of Directors	March 5, 2019
/s/ Patrick Machado Patrick Machado	Member of the Board of Directors	March 5, 2019
/s/ Robert J. Meyer Robert J. Meyer, MD	Member of the Board of Directors	March 5, 2019
/s/ Fred A. Middleton		

Fred A. Middleton	Member of the Board of Directors	March 5, 2019
/s/ Ronald C. Renaud Jr. Ronald C. Renaud Jr.	Member of the Board of Directors	March 5, 2019