CHIMERIX INC
Form 10-K
March 02, 2017

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, 2016
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 and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted 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 and post 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 or a smaller reporting company. See definitions of "large accelerated filer", "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act.:

Large accelerated filer o Accelerated filer x Non-accelerated filer o Smaller reporting company 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 30, 2016 was $125,692,357.*

The number of outstanding shares of the registrant's common stock, par value $0.001 per share, as of February 23, 2017 was 46,555,533.

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, 2016 are incorporated by reference into Part III of this report……	III

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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, 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 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 (AdV), and the human herpesviruses. We are also advancing the development of CMX521 for the treatment and prevention of norovirus. In addition, we have an active discovery program focusing on viral targets for which limited or no therapies are currently available.

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 1,000 patients treated 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), treatment of serious AdV infection and disease, treatment of smallpox, and treatment of BK virus (BKV) infection in kidney and HCT 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.

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 with 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.

The results of our AdVise trial, described further below, demonstrate:
1) a rapid decline in AdV viral load following oral administration of brincidofovir,
2) a correlation of rapid virologic response with improved survival, and

3) higher survival in patients identified with localized or asymptomatic infection compared with those who had advanced AdV disease, higher viral loads, and infection of multiple organ systems.

i.The AdVise Trial

The AdVise trial, conducted between March 2014 and April 2016, was an open-label, multicenter study designed to evaluate the efficacy, safety and overall tolerability of oral brincidofovir for the treatment of adenovirus infection. Pediatric and adult subjects were assigned to one of three cohorts:

- Cohort A, comprised of allogeneic HCT recipients with asymptomatic or limited AdV infection;
- Cohort B, comprised of allogeneic HCT recipients with disseminated adenovirus disease; and
- Cohort C, comprised of autologous HCT recipients, solid organ transplant recipients and other patients with serious AdV infections.

All subjects were to receive 12 weeks of oral brincidofovir and were followed for at least 36 weeks. On February 23, 2017, a final analysis was presented which included 158 allogeneic HCT recipients assigned to Cohorts A (23 adult and 42 pediatric patients) and B (35 adult and 58 pediatric patients).

In the AdVise trial, declines in AdV viral load of ≥2 $\log_{10}$ c/mL or below the limit of detection at week four were observed in 76 percent of pediatric patients and 45 percent of adult patients. Notably, this antiviral effect was observed even in HCT recipients who did not yet have immune recovery. In Cohort A, 55 percent of patients with baseline low immunity (CD4 counts <50 cells/ìL) achieved ≥2 $\log_{10}$ c/mL decline or undetectable AdV at week 4. In Cohort B, 52 percent of patients with baseline low immunity achieved ≥2 $\log_{10}$ c/mL decline or undetectable AdV over the same period of time.

In patients with disseminated disease, rapid virologic response, defined as undetectable AdV viremia at week 6, was associated with nearly double the survival rate and lower adenovirus-associated mortality compared with subjects who did not have an antiviral response, as summarized in the table below.

		Mortality		AdV-Associated Mortality
Pediatric	Responder*	7/28 (25%)	p=0.031	1/28 (4%)
	Non-responder	7/13 (54%)		2/13 (15%)
Adult	Responder*	5/10 (50%)	p=0.0004	0/10 (0%)
	Non-responder	13/14 (93%)		10/14 (71%)

*Responders defined as subjects with baseline AdV viremia still on study at week 6 who had undetectable plasma AdV at week 6; non-responders defined as subjects who did not achieve the specified cut-off. A Cox model incorporating age group was used to compare mortality at 36 weeks in responders and non-responders.

Diarrhea was the most commonly reported treatment-emergent adverse event in AdVise Cohorts A and B, reported at 38 percent of adult and 43 percent of pediatric HCT recipients. Treatment discontinuations related to diarrhea in Cohorts A and B occurred in 5 percent of adult and 6 percent of pediatric patients.

Many subjects enrolled in AdVise, particularly in the first few months of the study, began therapy at a point when they had multiple organ failure or other diagnoses likely to negatively impact their ability to survive the first four weeks of treatment. There was therefore a significant improvement in survival observed for subjects enrolled in the fourth quartile who were begun on brincidofovir with lower viral loads and a shorter time from AdV diagnosis to initiation of treatment. Conditions such as respiratory failure requiring mechanical ventilation, renal failure or relapse of underlying malignancy that are associated with short term mortality are planned to be exclusionary for Study 999.

The rapid virologic responses observed in AdVise, the correlation of antiviral response with improved survival, and the potential for shorter courses of therapy in patients whose AdV infection is identified while the infection is localized/asymptomatic support further study of short course oral brincidofovir therapy in pediatric patients with AdV infection following allogeneic HCT. We anticipate conducting Study 999 (discussed below) as a next step.

ii.Study 999 and the AdVance Study

Study 999 is anticipated to be a small (approx. 140 patients) comparative clinical trial designed to study brincidofovir compared with the standard-of-care in pediatric HCT-recipients with AdV viremia detected in the first 100 days following transplant. The primary endpoint of Study 999 is the proportion of subjects with undetectable plasma AdV at week 4. Study 999 is designed to leverage key learnings from AdVise.

Data from AdVise demonstrated that, overall, pediatric patients were more likely than adult patients to be diagnosed with AdV earlier in the post-transplant period, likely due to regular screening for AdV in place in many pediatric

transplant centers. With regular screening, AdV viremia can be detected quickly after reactivation, at a point when viral loads are lower and more likely to be cleared within the first 2-4 weeks of brincidofovir therapy.

Due to the low incidence of AdV infection in adult HCT recipients, adults are generally not screened for AdV and are thus diagnosed with AdV only once symptomatic, and often with higher viral loads and more significant end-organ disease. Even with rapid virologic response to BCV, adults enrolled in AdVise succumbed to other opportunistic infections or organ failure.

If successful, Study 999 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.

We expect to initiate enrollment of Study 999 in the second half of 2017.

We are also currently conducting AdVance, a retrospective, observational study of the current standard-of-care for treatment of AdV in France, Germany, Italy, Spain, and the United Kingdom. We expect data from AdVance to describe the incidence and outcomes associated with standard of care treatment of AdV infection, supporting the need for new therapeutic options.

B. Oral Brincidofovir for Treatment of Smallpox

We are collaborating with the Biomedical Advanced Research and Development Authority (BARDA) for the development of brincidofovir as a potential medical countermeasure for smallpox. Efficacy is to be demonstrated via two animal model studies under the FDA's Animal Rule. Following completion of the second animal efficacy study, we plan to meet with the FDA to discuss any additional required data for a regulatory decision.

During 2016, we provided regulators with a summary of the clinical safety and tolerability of the intended three week course of oral brincidofovir in healthy adults and immunocompromised adults and children, as well as the final study report for the rabbitpox efficacy study of brincidofovir. In this well-characterized model of smallpox, animals were administered a lethal inoculum of rabbitpox virus, and monitored for clinical signs of disease. Following the onset of fever, animals were randomized to receive placebo, immediate brincidofovir, or brincidofovir after a delay of 24, 48, or 72 hours. In this study, brincidofovir administered immediately following the first clinical evidence of infection (fever) demonstrated 100 percent survival. Animals treated with brincidofovir 24 or 48 hours following confirmation of infection demonstrated a 68 percent reduction in mortality compared to animals that received placebo, a group that had less than 50 percent survival. Brincidofovir administered immediately after confirmed infection, or after a 24 or 48 hour delay, resulted in statistically significant ($p<0.05$) improved mortality compared with the animals that received placebo. Although not statistically significant, there was a numerically improved survival in the animals that began BCV 72 hours after confirmed infection.

Through our continuing development contract with BARDA, we are conducting final confirmatory studies prior to conducting the pivotal efficacy study in the mouse model of smallpox infection (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.

In October 2016, we were notified that the European Medicines Agency's Committee for Orphan Medicinal Products issued a positive opinion for an Orphan Designation for brincidofovir for the treatment of smallpox.

C. Oral Brincidofovir Expanded Access Program

We continue to fulfill requests for orally administered brincidofovir via our expanded access programs. In 2016, we granted over 300 requests for AdV alone, highlighting the continued unmet need in this area.

II. Intravenous (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. Data from preclinical and clinical testing, summarized above, support the continued development of oral brincidofovir for short course treatment of smallpox

and AdV. In 28-day animal studies and single dose administration in healthy subjects, IV BCV has shown the potential for less gastrointestinal (GI) injury compared to oral brincidofovir, even with higher plasma drug concentrations and longer-term dosing.

A. Preclinical Assessments of IV Brincidofovir in Rats

In 2016, we announced the results of a 28-day toxicology study of IV brincidofovir in rats, and a single dose study of radiolabeled brincidofovir administered orally or via IV administration. Data from the radiolabeled brincidofovir study showed that oral administration of brincidofovir provided consistent drug exposure to organs that are often the target of viral infection, such as the liver and kidney, but delivered much higher drug exposures to the small intestine. In contrast, IV brincidofovir demonstrated consistent drug exposure levels to key target organs, while avoiding overexposure in the small intestine. Importantly, IV brincidofovir resulted in higher central nervous system concentrations, which may support testing of this formulation in viral infections that occur in difficult-to-reach compartments, including the brain.

The 28-day toxicology study of IV brincidofovir in rats achieved higher plasma concentrations than had been achieved with oral drug administration, and importantly did not demonstrate the gastrointestinal injury characterized across multiple species following oral brincidofovir administration.

B. IV Brincidofovir Single Ascending Dose Study in Healthy Subjects

In this Phase 1 study, a total of 40 healthy subjects have been randomized to receive either a single dose of IV BCV or IV placebo in one of four cohorts:

- Cohort 1: IV BCV 10 mg (n=6) or placebo (n=2);
- Cohort 2: IV BCV 25 mg (n=6) or placebo (n=2);
- Cohort 3: IV BCV 50 mg given over 2 hours (n=9) or placebo (n=3); and
- Cohort 4: IV BCV 50 mg given over 4 hours (n=9) or placebo (n=3).

In this ongoing blinded study, a favorable safety and tolerability profile has been observed in all three cohorts completed to date. Grade 1-2 (on a scale of Grade 1-5) safety laboratory changes were observed in some subjects in the first three dosing cohorts; none were considered clinically significant. No Grade 3 or higher safety laboratory abnormalities were observed for any subjects receiving IV study drug in Cohorts 1, 2 and 3. In Cohort 3, IV BCV 50 mg or placebo, mild Adverse Events (AEs) were reported that possibly were related to study-drug included: a single lower gastrointestinal event of loose stools was reported in one subject, and two other subjects each reported a mild headache that spontaneously resolved. In addition, three subjects had bruising at the site of the IV catheter. IV BCV 50 mg provided plasma drug exposures higher than achieved with oral BCV dosing, and in the range of exposures targeted for treatment indications such as for BK nephropathy.

Cohort 4 will explore IV BCV 50 mg or placebo over a longer period of infusion. Complete clinical and pharmacokinetic data from all four cohorts are expected to be reported in the first half of 2017.

C. Additional Studies Planned

Following completion of the Single Ascending Dose study of IV BCV, we anticipate conducting a Multiple Ascending Dose (MAD) study of IV brincidofovir in healthy subjects, as well as dose-ranging studies of IV BCV in patients with active viral infections including CMV and/or BKV. Given the broad-spectrum antiviral activity of brincidofovir and the known frequency of multiple DNA viral infections in HCT recipients, we intend to conduct a multi-viral prevention study in high-risk HCT recipients which could initiate in 2018 and could support the first indication for IV brincidofovir. Following the dose-ranging studies in active viral infections, we anticipate conducting pivotal study(ies) in treatment of BK viremia in order to prevent BK-associated nephropathy in kidney transplant recipients. In addition, the improved drug concentrations in the central nervous system (CNS) achieved with IV brincidofovir could support the study of IV brincidofovir in viral CNS infections such as herpes encephalitis, JC virus infection, and CMV infection, which has recently been described to be associated with glioblastoma.

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.

Chronic norovirus infection is increasingly being diagnosed in immune compromised patients. Approximately 15-20 percent of HCT and SOT recipients are diagnosed with norovirus within the first 1-2 years after transplant, a diagnosis that has been associated with chronic diarrhea, electrolyte disturbances, and graft rejection.

Toxicology studies of CMX521conducted to date suggest a favorable safety profile. We are currently conducting final preclinical studies of CMX521 in animals. These studies are required to file an Investigational New Drug application (IND) that would allow clinical testing of CMX521 in humans. Assuming we receive positive results from our ongoing preclinical testing, we expect an IND could be filed during the latter half of 2017.

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, the Company 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.

Our Chemical Library and Lipid Conjugate Technology

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 adenovirus 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 are currently screening the library for activity against multiple viruses including CMV, hepatitis B, and norovirus. Additionally, we are exploring the potential utility of library compounds for the treatment of cancer.

Our Strategy

Our strategy is to discover, develop and commercialize novel therapeutics in areas of significant unmet medical need. Our primary initial focus is leveraging the broad-spectrum profile of brincidofovir to address the multiple DNA viral infections common in transplant recipients and patients with relative immune compromise.

The key components of our strategy are:

- Advance Oral and IV Formulations of Brincidofovir for the Prevention and Treatment of DNA Virus Infections in HCT and SOT Recipients. We are in the process of initiating a small comparative clinical trial designed to study the effect of brincidofovir versus standard of care in pediatric patients with AdV infection following allogeneic HCT (Study 999). The initial focus of the study will be in European clinical trial sites. If successful, Study 999 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. We plan to discuss the design and conduct of this study with the FDA as well. We expect to initiate enrollment of Study 999 in the second half of 2017, which could lead to data as early as the end of 2018 and a potential approval in the EU by 2020.

Following completion of the Single Ascending Dose study of IV BCV, we anticipate conducting a Multiple Ascending Dose (MAD) study of IV brincidofovir in healthy subjects, as well as dose-ranging studies of IV BCV in patients with active viral infections including CMV and/or BKV. Given the broad-spectrum antiviral activity of brincidofovir and the known frequency of multiple DNA viral infections in HCT recipients, we intend to conduct a multi-viral prevention study in high-risk HCT recipients which could initiate in 2018 and could support the first indication for IV brincidofovir.

- Progress Development of Brincidofovir as a Medical Countermeasure for the Treatment of Smallpox. We have conducted efficacy studies under the FDA's Animal Rule to demonstrate the impact of immediate or delayed brincidofovir in a validated model of smallpox infection. We are working with BARDA on design elements of a pivotal efficacy study in a second animal model of smallpox. If we obtain positive results from such a study, we

would expect to engage the FDA in discussions about what additional studies, if any, would be required for marketing authorization of brincidofovir for the treatment of smallpox.

- Develop CMX521 for the Prevention and Treatment of Norovirus. We are currently conducting final preclinical studies of CMX521 in animals. These studies are required to file an Investigational New Drug application (IND) that would allow clinical testing of CMX521 in humans. Assuming we receive positive results from our ongoing preclinical testing, we expect an IND could be filed during the latter half of 2017.

- Discover and Develop Additional Product Candidates to Strengthen our Product Portfolio. We have an active discovery and preclinical development program focused on identifying and developing new compounds that can be used to treat diseases for which no current therapeutic option exists or which otherwise continue to have high unmet medical need. We intend to leverage our knowledge and experience of nucleoside analogs to advance compounds in the Chimerix Chemical Library through IND-enabling studies and potential clinical development and/or partnerships. In addition, we are exploring other potential product opportunities based on the ability of our proprietary lipid conjugate technology to significantly improve the drug profile of molecules with limitations in safety or delivery.

- Evaluate 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 1,071,429 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 (HHS) 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 funding for the performance of the second option segment, which is scheduled to end on June

30, 2017. On September 11, 2015, BARDA exercised option segment three, which provided approximately $13 million in funding for the performance of the segment, increasing the total funding of the contract, including this option segment, from approximately $53 million to approximately $66.1 million, and provided that the period of performance for option segment three would begin on September 11, 2015 and end on March 31, 2017. As of December 31, 2016, we had recognized revenue in aggregate of $51.7 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 Department of Health and Human Services, 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 related request for proposal (RFP) to us 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. 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 Food and Drug Administration's Animal 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 PD) 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 U.S. HCT transplant centers 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 (or CMV infection), we believe it is possible for us to commercialize brincidofovir in the United States, and potentially Canada. 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 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:

- Vistide® (cidofovir for injection), marketed by Gilead Sciences, Inc. and 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, an anti-CMV drug being developed for the prevention of CMV infections in adult HCT recipients pursuant to an exclusive worldwide license agreement between AiCuris GmbH & Co. KG and Merck;
- maribavir, an antiviral owned by Shire, 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
- ASP0113 (TransVax), a CMV prevention vaccine, licensed to Astellas Pharma Inc. from Vical Incorporated and in development by Astellas and Vical; 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 23, 2017, our worldwide patent portfolio included:

- over 133 patents or patent applications that we own or have in-licensed from academic institutions, related to brincidofovir and CMX157, which represented a slight increase over the number of patents and patent applications in our patent portfolio at the end of fiscal 2015;
- 21 patents and patent applications related to our agreement with the University of Michigan regarding our proprietary Chemical Library; and

- 71 US and foreign exclusively and jointly owned patents, and 62 U.S., PCT, and foreign applications relating to brincidofovir or CMX157.

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 manufacturing process to our selected contractor that will produce commercial supplies. We are in the process of transferring our current commercial tablet manufacturing process to our selected contractor that will produce commercial supplies. We will begin validation of these processes in 2017. 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 European Medicines Agency (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 New Drug Application (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. 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 (discussed below).

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.

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 European Medicines Agency (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. Each Orphan Designation carries the potential for one market exclusivity for a particular indication. A medicine that has several separate Orphan Designations for different indications can have several separate market exclusivities if these refer to separate designated conditions.

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 Paediatric Committee and opinion from the CHMP.

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.

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 Department of Health and Human Services, the 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 is 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 (ACA), as amended by the Health Care and Education Affordability Reconciliation Act of 2010, 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 is expected to expand and increase 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 many of the ACA’s reforms require the promulgation of detailed regulations to implement the statutory provisions, which has not yet occurred. In addition, although the United States Supreme Court has upheld the constitutionality of most of the ACA, some states have indicated that they intend not to implement certain sections of the ACA and some members of the U.S. Congress are still working to repeal the ACA. These challenges add to the uncertainty of the effects of the 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 Department of Health and Human Services 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 civil monetary penalties of up to $150,000 per

year (up to $1 million per year for “knowing failures”) 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.

In January, Congress voted to adopt a budget resolution for fiscal year 2017, or the Budget Resolution, that authorizes the implementation of legislation that would repeal portions of the ACA. The Budget Resolution is not a law, however, it is widely viewed as the first step toward the passage of legislation that would repeal certain aspects of the ACA. Further, on January 20, 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA

to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. Congress also could consider subsequent legislation to replace elements of the ACA that are repealed.

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.

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, 2016, we had 87 full-time employees. Of these employees, 61 employees are engaged in research and development activities and 26 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 29,053 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 June 2018 and August 2018, 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 $76.4 million, $117.4 million and $59.3 million for the twelve months ended December 31, 2016, 2015 and 2014, respectively. As of December 31, 2016, we had an accumulated deficit of approximately $415.8 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 adenovirus (AdV) infection;
- continue the development of brincidofovir for the prevention or treatment of cytomegalovirus (CMV), AdV, BK virus, and other viral indications in hematopoietic cell transplant (HCT) recipients, solid organ transplant recipients and other patient populations;
- continue the development of brincidofovir for the treatment of smallpox as a medical countermeasure;

- advance the development of an intravenous (IV) formulation of brincidofovir;
- obtain regulatory approvals for brincidofovir;
- scale-up manufacturing capabilities to commercialize brincidofovir for any indications for which we receive regulatory approval;
- conduct IND-enabling studies and initiate clinical development of CMX521 for norovirus;
- 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 U.S. Food and Drug Administration (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.

We have undertaken a review of our overall development plan for brincidofovir. We anticipate that we will need to conduct one or more clinical trials in order to attain FDA and/or foreign regulatory approval of brincidofovir. Because of the numerous risks

and uncertainties associated with pharmaceutical product development, we are unable to predict the timing or amount of any increase in our anticipated development costs that will result from any additional trials.

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. As we increase development with the IV formulation, with CMX521 for norovirus, and with our BARDA activities, we currently expect research and development expenses to trend upward modestly in 2017. In addition, we presently continue to provide brincidofovir for the treatment of AdV infection through our expanded access trial (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. For example, 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 requires us to perform studies or trials in addition to those that we currently anticipate. 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.

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 in light of an absence of a mortality benefit observed, when results were compared to data from Study 305, our historical matched control study, we will be required to conduct one or more additional prospective, controlled trials of brincidofovir in AdV.

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; and
- obtaining, maintaining, enforcing and defending intellectual property rights and claims.

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.

In light of the numerical difference in mortality observed in SUPPRESS and the absence of a mortality benefit observed when results from our AdVise study were compared to data from Study 305, our historical matched control study, it is anticipated that regulatory approval of brincidofovir for the treatment of AdV will require one or more additional prospective controlled studies of brincidofovir in patients with AdV. 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.

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.

It is our intention to continue development of brincidofovir for the treatment of smallpox through assessment of efficacy in animal models of orthopox virus infections.

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 orthopox 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 orthopox 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.

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.

For example, in light of the results from our Phase 3 SUPPRESS and open-label AdVise trials of brincidofovir we anticipate that we will need to conduct one or more additional studies of brincidofovir, and the clinical studies we design and/or submit may not be approved. 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 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 required institutional review board approval at 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 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.

For example, 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.

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 risk evaluation and mitigation strategy (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 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 current good manufacturing practices (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 are 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 civil monetary penalties, including 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 its 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, clearinghouses and healthcare providers;
- the federal Food, Drug and Cosmetic Act (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 and Health Care and Education Reconciliation Act of 2010 (collectively, the Health Care Reform Law), and its implementing regulations, which requires manufacturers of drugs, devices, biologicals and medical supplies to report to the U.S. Department of Health and Human Services 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; and 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.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may 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, 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 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 Health Care Reform Law 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 Health Care Reform Law 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. We will not know the full effects of the Health Care Reform Law until applicable federal and state agencies issue regulations or guidance under the new law.

Although it is too early to determine the effect of the Health Care Reform Law, the new 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 been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. Recently, the U.S. House of Representatives and Senate passed legislation, which, if signed into law by President Trump, would repeal certain aspects of the Health Care Reform Law. Further, on January 20, 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the Health Care Reform Law to waive, defer, grant exemptions from, or delay the implementation of any provision of the Health Care Reform Law that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. Congress also could consider subsequent legislation to replace elements of the Health Care Reform Law that are repealed. We are not sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be.

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 bills 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.

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 processes 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 process, 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, which follows the International Conference on 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 of alternative treatments;
- pricing and cost-effectiveness;
- effectiveness of our or any future collaborators' 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 or 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 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;
- 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 treat AdV and/or CMV include and are not limited to:

- Vistide® (cidofovir for injection), marketed by Gilead Sciences, Inc. and 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

- investigational patient-specific T-cell therapies.

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

- letermovir, an anti-CMV drug being developed pursuant to an exclusive worldwide license agreement between AiCuris GmbH & Co. KG and Merck;
- maribavir (SHP620) from Shire for CMV infections in transplant recipients;
- ASP0113 (TransVax), a CMV prevention vaccine, licensed to Astellas Pharma Inc. from Vical Incorporated and in development by Astellas and Vical; 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. 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 reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and third-party payers, such as private health insurers, hospitals and health maintenance organizations, 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. Government authorities and these 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.

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 The Regents of the University of California (UC), which we believe cover brincidofovir. We also have an exclusive license to certain patents covering inventions of the Regents of the University of Michigan (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 June 2017 and March 2017, 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 segment is 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.

At present, certain activities that are included in Option Segments 2 and 3 of our contract with BARDA are forecasted to end later than the current end of the period of performance of those contract segments (i.e. later than June 30, 2017 and March 31, 2017, respectively). We plan to request no-cost extensions for each contract segment before the scheduled end of the period of performance. If we are unable to reach agreement with BARDA on a no-cost extension to either, or both, of these segments our ability to receive revenues under the contract will be materially impaired.

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 related request for proposal (RFP) to us entitled “2015 Procurement of a Second Smallpox Antiviral Drug for the Strategic National Stockpile." Notwithstanding the issuance of the RFP, there can be no assurances that we will enter into a contract with BARDA to act as the sole supplier for the procurement of brincidofovir for the treatment of smallpox.

Before we can enter into the 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. In August 2015, we submitted a response to the RFP and we subsequently engaged in discussions with BARDA regarding our response. 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 Food and Drug Administration’s Animal rule.

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 Department of Health and Human Services (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 Federal Civil False Claims Act (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 up to $11,000 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 and criminal 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 illness 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 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 materially harm our business.

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 and civil 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 occurred in December 2015, a large percentage of the options held by our employees are underwater. As of December 31, 2016, greater than 90% of all outstanding options had an exercise price below 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. In

May 2016 in order to address the issue of employee retention we granted a total of 1.2 million restricted stock units to employees and executives with vesting over 18 and 36 months respectively. 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;

- 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 in operate, 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.

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, 2016, our executive officers, directors, 5% stockholders (known to us through available information) and their affiliates beneficially owned approximately 39% 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.

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

Under Section 382 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an "ownership change," generally defined as a greater than 50 percent change (by value) in its equity ownership over a three year period, the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes (such as research tax credits) to offset its post-change income 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, 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.

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 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 requirements. 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 29,053 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 June 2018 and August 2018, 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, 2016	
	High	Low
First Quarter	$9.72	$4.36
Second Quarter	$6.47	$3.50
Third Quarter	$5.96	$3.71
Fourth Quarter	$5.64	$3.66

	Year Ended December 31, 2015	
	High	Low
First Quarter	$43.41	$34.51
Second Quarter	$47.46	$33.37
Third Quarter	$58.04	$35.62
Fourth Quarter	$43.37	$6.43

Stock Performance Graph[(1)]

The following graph shows a comparison from April 11, 2013 through December 31, 2016 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 April 11, 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 4/11/2013 (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 23, 2017, there were 31 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, 2016, 2015, and 2014 and the selected consolidated balance sheet data as of December 31, 2016 and 2015 from our audited consolidated financial statements and related notes appearing elsewhere in this Annual Report.

	Years Ended December 31,				
Consolidated Statement of Operations and Comprehensive Loss Data	2016	2015	2014	2013	2012
Revenues:					
Contract revenue	$5,702	$9,214	$4,040	$4,370	$16,275
Collaboration and licensing revenue	—	1,548	—	—	17,445
Total revenues	5,702	10,762	4,040	4,370	33,720
Operating expenses:					
Research and development	58,647	97,717	45,379	24,662	30,106
General and administrative	25,007	31,296	17,527	8,327	6,397
Total operating expenses	83,654	129,013	62,906	32,989	36,503
Loss from operations	(77,952)	(118,251)	(58,866)	(28,619)	(2,783)
Other income (expense):					
Interest income (expense), net	1,562	879	(446)	(1,236)	(776)
Fair value adjustments to preferred stock warrant liability	—	—	—	(6,590)	(847)
Net loss	(76,390)	(117,372)	(59,312)	(36,445)	(4,406)
Accretion of redeemable convertible preferred stock	—	—	—	(34,108)	(4,357)
Net loss attributable to common shareholders	$(76,390)	$(117,372)	$(59,312)	$(70,553)	$(8,763)
Net loss per share, basic and diluted	$(1.65)	$(2.67)	$(1.80)	$(3.65)	$(5.75)
Weighted-average shares outstanding, basic and diluted	46,267,064	43,878,326	33,003,714	19,307,422	1,524,628

	Years Ended December 31,				
Consolidated Balance Sheet Data	2016	2015	2014	2013	2012
Cash and cash equivalents	$51,463	$20,605	$128,462	$109,976	$19,906
Short-term investments, available-for-sale (1)	180,558	199,729	106,114	—	9,849
Working capital	226,360	208,658	220,390	102,802	23,931
Long-term investments (1)	47,407	124,040	52,973	—	—
Total assets	286,770	355,992	291,878	113,387	32,031
Loan payable, net, current portion (2)	—	—	4,296	5,573	4,753
Loan payable, net, less current portion (2)	—	—	—	4,294	9,867
Redeemable convertible preferred stock warrant liability	—	—	—	—	7,512
Redeemable convertible preferred stock	—	—	—	—	107,723
Accumulated deficit	(415,804)	(339,414)	(222,042)	(162,730)	(101,032)
Total stockholders' equity (deficit)	$276,224	$335,459	$274,636	$98,539	$(101,031)

(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. We are also advancing the development of CMX521 for the treatment and prevention of norovirus. In addition, we have an active discovery program focusing on viral targets for which limited or no therapies are currently available.

Recent Developments

Preliminary Data from Ongoing Phase 1 Single Ascending Dose Study of Intravenous BCV in Healthy Subjects

On March 2, we presented preliminary data from the ongoing Phase 1 Single Ascending Dose study of IV brincidofovir in which a total of 40 healthy subjects have been randomized to receive either a single dose of IV brincidofovir or IV placebo in one of four cohorts:

- Cohort 1: IV BCV 10 mg (n=6) or placebo (n=2);
- Cohort 2: IV BCV 25 mg (n=6) or placebo (n=2);
- Cohort 3: IV BCV 50 mg given over 2 hours (n=9) or placebo (n=3); and
- Cohort 4: IV BCV 50 mg given over 4 hours (n=9) or placebo (n=3).

In this ongoing blinded study, a favorable safety and tolerability profile has been observed in all three cohorts completed to date. Grade 1-2 (on a scale of Grade 1-5) safety laboratory changes were observed in some subjects in the first three dosing cohorts; none were considered clinically significant. No Grade 3 or higher safety laboratory abnormalities were observed for any subjects receiving IV study drug in Cohorts 1, 2 and 3. In Cohort 3, IV BCV 50 mg or placebo, mild Adverse Events (AEs) were reported that possibly were related to study-drug included: a single lower gastrointestinal event of loose stools was reported in one subject, and two other subjects each reported a mild headache that spontaneously resolved. In addition, three subjects had bruising at the site of the IV catheter. IV BCV 50 mg provided plasma drug exposures higher than achieved with oral BCV dosing, and in the range of exposures targeted for treatment indications such as for BK nephropathy.

Cohort 4 will explore IV BCV 50 mg or placebo over a longer period of infusion. Complete clinical and pharmacokinetic data, from all four cohorts are expected to be reported in the first half of 2017.

Final Data from AdVise Trial

On February 23, 36-week data from the AdVise trial of BCV for the treatment of adenovirus infection in allogeneic hematopoietic cell transplant (HCT) recipients was presented at the combined annual meetings of the Center for International Blood & Marrow Transplant Research (CIBMTR) and the American Society for Blood and Marrow Transplantation (ASBMT) held February 22-26, 2017 in Orlando, FL.

The AdVise trial, conducted between March 2014 and April 2016, was an open-label, multicenter study designed to evaluate the efficacy, safety and overall tolerability of oral brincidofovir for the treatment of adenovirus infection. Pediatric and adult subjects were assigned to one of three cohorts:

- Cohort A, comprised of allogeneic HCT recipients with asymptomatic or limited adenovirus infection;
- Cohort B, comprised of allogeneic HCT recipients with disseminated adenovirus disease; and
- Cohort C, comprised of autologous HCT recipients, solid organ transplant recipients and other patients with serious adenovirus infections.

All subjects were to receive 12 weeks of oral brincidofovir and were followed for at least 36 weeks. The final analysis includes 158 allogeneic HCT recipients assigned to Cohorts A (23 adult and 42 pediatric patients) and B (35 adult and 58 pediatric patients).

In the AdVise trial, declines in AdV viral load of ≥2 $\log_{10}$ c/mL or below the limit of detection at week four were observed in 76 percent of pediatric patients and 45 percent of adult patients. Notably, this antiviral effect was observed even in HCT recipients who did not yet have immune recovery. In Cohort A, 55 percent of patients with baseline low immunity (CD4 counts <50 cells/ìL) achieved ≥2 $\log_{10}$ c/mL decline or undetectable AdV at week 4. In Cohort B, 52 percent of patients with baseline low immunity achieved ≥2 $\log_{10}$ c/mL decline or undetectable AdV over the same period of time.

In patients with disseminated disease, rapid virologic response, defined as undetectable AdV viremia at week 6, was associated with nearly double the survival rate and lower AdV-associated mortality compared with subjects who did not have an antiviral response, as summarized in the table below.

		Mortality		AdV-Associated Mortality
Pediatric	Responder*	7/28 (25%)	p=0.031	1/28 (4%)
	Non-responder	7/13 (54%)		2/13 (15%)
Adult	Responder*	5/10 (50%)	p=0.0004	0/10 (0%)
	Non-responder	13/14 (93%)		10/14 (71%)

*Responders defined as subjects with baseline AdV viremia still on study at week 6 who had undetectable plasma AdV at week 6; non-responders defined as subjects who did not achieve the specified cut-off. A Cox model incorporating age group was used to compare mortality at 36 weeks in responders and non-responders.

Diarrhea was the most commonly reported treatment-emergent adverse event in AdVise Cohorts A and B, reported at 38 percent of adult and 43 percent of pediatric HCT recipients. Treatment discontinuations related to diarrhea in Cohorts A and B occurred in 5 percent of adult and 6 percent of pediatric patients.

Many subjects enrolled in AdVise, particularly in the first few months of the study, began therapy at a point when they had multiple organ failure or other diagnoses likely to negatively impact their ability to survive the first four weeks of treatment. There was therefore a significant improvement in survival observed for subjects enrolled in the fourth quartile who were begun on brincidofovir with lower viral loads and a shorter time from AdV diagnosis to initiation of treatment. Conditions such as respiratory failure requiring mechanical ventilation, renal failure or relapse of underlying malignancy that are associated with short term mortality are planned to be exclusionary for Study 999.

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 $17.5 million and $13 million in expense reimbursement and fees, respectively. The second option segment is scheduled to end on June 30, 2017 and the third option segment is scheduled to end on March 31, 2017. As of December 31, 2016, we had recognized revenue in aggregate of $51.7 million with respect to the base performance segment and the first three extension periods.

In July 2012, we entered into a collaboration and licensing agreement with Merck, Sharp & Dohme Corporation (Merck). The agreement provided for various types of payments, including a $17.5 million non-refundable upfront license fee, contingent event-based milestone payments and future royalties on net product sales. We recognized the

upfront license fee payment from Merck as revenue for the year ended December 31, 2012, as our remaining performance obligations under the contract were not considered substantive. We did not recognize any revenue under this agreement for the years ended December 31, 2013 and 2014. The license agreement with Merck was terminated in May 2014.

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, the Company converted its shares of ContraVir Series B Convertible Preferred Stock into 1,071,429 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 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, 2016, we have incurred approximately $355.4 million in research and development expenses, of which $315.6 million relates to our development of brincidofovir. These costs were largely related to the conduct of our clinical trials, including most recently our two 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,		
	2016	2015	2014
Direct research and development expenses	$31,415	$70,348	$31,392
Research and development personnel costs	22,172	22,269	11,235
Indirect research and development expenses	5,060	5,100	2,752
Total research and development expenses	$58,647	$97,717	$45,379

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), 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 orthopox virus 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 performed 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.

Following conclusion of our Phase 3 SUPPRESS trial and our AdVise study, and the closing of our SUSTAIN and SURPASS trials in kidney transplant recipients, research and development expenses significantly decreased in 2016. As we increase development with the IV formulation, with CMX521 for norovirus, and with our BARDA activities, we currently expect research and development expenses to trend upward modestly in 2017.

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.

General and administrative expenses decreased in 2016, driven primarily by a reduction in expenses related to commercial preparations and other cost saving efforts. As we begin to increase these expenses again, we currently expect general and administrative expense to trend upward modestly in 2017.

Interest Income (Expense), Net

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

Interest expense consists primarily of interest accrued or paid on amounts outstanding under our Loan and Security Agreement (LSA) with Silicon Valley Bank (SVB) and MidCap Financial SBIC, LP (MidCap). In January 2012, we borrowed $3.0 million under the LSA, and in September 2012, we borrowed an additional $12.0 million. In October 2015, the loan was paid in full.

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 $16.2 million, $13.0 million and $4.4 million was recognized in the years ended December 31, 2016, 2015 and 2014, respectively. The share-based compensation expense recognized included expense for stock options, restricted stock units (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.

Equity instruments issued to non-employees are periodically revalued as the equity instruments vest and are recognized as expense over the related service period.

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, 2016 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

We derive our revenues from two sources: contracts and grants, and collaborations and licensing. Contract and grant revenue is revenue generated pursuant to federal contracts and other awarded grants. Collaboration and licensing revenue is revenue related to license and collaboration agreements. We recognize revenue in accordance with the criteria outlined in the Securities and Exchange Commission (SEC)’s Topic 13 and Accounting Standards Codification

(ASC) 605-25 and by the Financial Accounting Standards Board. Following these accounting pronouncements, revenue is recognized when all four of the following criteria are met: (i) persuasive evidence of an arrangement exists; (ii) delivery of the products and/or services has occurred and risk of loss has passed; (iii) the selling price is fixed or determinable; and (iv) collectability is reasonably assured.

For arrangements that involve the delivery of more than one element, each product, service and/or right to use assets is evaluated to determine whether it qualifies as a separate unit of accounting. This determination is based on whether the deliverable has “stand-alone value” to the customer. The consideration that is fixed or determinable is then allocated to each separate unit of accounting based on the relative selling prices of each deliverable. The consideration allocated to each unit of accounting is recognized as the related goods and services are delivered, limited to the consideration that is not contingent upon future deliverables. If the arrangement constitutes a single unit of accounting, the revenue recognition policy must be determined for the entire arrangement and the consideration received is recognized over the period of inception through the date the last deliverable within the single unit of accounting is expected to be delivered. Revisions to the estimated period of recognition are reflected in revenue prospectively.

Non-refundable upfront fees are recorded as deferred revenue and recognized into revenue as license fees from collaborations on a straight-line basis over the estimated period of our substantive performance obligations. If we do not have substantive performance obligations, we recognize non-refundable upfront fees into revenue through the date the deliverable is satisfied. Analyzing the arrangement to identify deliverables requires the use of judgment, and each deliverable may be an obligation to deliver services, a right or license to use an asset, or another performance obligation.

Milestone payments are recognized when earned, provided that (i) the milestone event is substantive, (ii) there is no ongoing performance obligation related to the achievement of the milestone earned, and (iii) it would result in additional payments. Milestone payments are considered substantive if all of the following conditions are met: the milestone payment is non-refundable; achievement of the milestone was not reasonably assured at the inception of the arrangement; substantive effort is involved to achieve the milestone; and the amount of the milestone appears reasonable in relation to the effort expended, the other milestones in the arrangement and the related risk associated with the achievement of the milestone. Contingent based event payments we may receive under a license or collaboration agreement will be recognized when received.

From our inception through December 31, 2016, we have not generated any revenue from product sales. For the same period, we have generated $89.1 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.

In July 2012, we entered into a collaboration and licensing agreement with Merck, Sharp & Dohme Corporation (Merck). The agreement provided for various types of payments, including a $17.5 million non-refundable upfront license fee, contingent event-based milestone payments and future royalties on net product sales. We recognized the upfront license fee payment from Merck as revenue for the year ended December 31, 2012, as our remaining performance obligations under the contract were not considered substantive. The contingent event-based payments pursuant to our agreement with Merck did not meet the definition of a milestone as achievement of the triggering event for such payments was based on the performance of Merck and not our performance. Therefore the milestone method was not applied to any such payments. We did not recognize any revenue under this agreement for the years ended December 31, 2014 and 2013. The license agreement with Merck was terminated in May 2014.

On December 17, 2014, we entered into a collaboration and license agreement with ContraVir Pharmaceuticals. 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. The upfront payment of 120,000 shares of ContraVir Series B Convertible Preferred Stock was valued at $1.5 million at the time of the agreement. We recorded this amount as deferred revenue, and upon completion of the transfer of the IND and technical know-how related to CMX157 in April 2015, we recognized the $1.5 million upfront payment as revenue. In September 2016, we converted our shares of ContraVir Series B Convertible Preferred Stock into 1,071,429 shares of ContraVir common stock.

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, 2016, 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 brokered certificates of deposit, 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 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 or expense, 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 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 interest income or expense, net. There were no such declines in value for the years ended December 31, 2016, 2015 and 2014.

We also analyze our investments in unconsolidated affiliates for impairment. This analysis consists of determining whether an expected loss in market value of an investment is other than temporary by evaluating the length of time and the extent to which the market value has been less than cost, the financial condition and near-term prospects of the unconsolidated affiliate, and our intent and ability to retain our investment for a period of time sufficient to allow for any anticipated recovery in market value. As the factors used in this analysis are difficult to predict and are subject to future events that may alter the assumptions, we may be required to recognize future impairment losses on our investments in unconsolidated affiliates.

Valuation of Share-Based Compensation

We record the fair value of share-based awards issued to employees as of the grant date as compensation expense. We recognize compensation expense over the requisite service period, which is equal to the vesting period. For non-employees, we also record the fair value of stock options as of the grant date as compensation expense. We then periodically re-measure the awards to reflect the current fair value at each reporting period until the non-employee completes the performance obligation or the date on which a performance commitment is reached. Expense is recognized over the related service period.

For the years ended December 31, 2016, 2015, and 2014, there was no non-employee share-based compensation expense. Employee 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:

	Years Ended December 31,		
	2016	2015	2014
Income Statement Classification:			
Research and development expense	$7,137	$5,578	$1,085
General and administrative expense	9,086	7,381	3,326
Total stock-based compensation expense	$16,223	$12,959	$4,411

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, 2016, 2015, and 2014 are set forth below:

Stock Options

	Years Ended December 31,		
	2016	2015	2014
Expected volatility	85.16%	66.89%	71.47%
Expected term (in years)	6.0	6.0	6.0
Weighted-average risk-free interest rate	1.70%	1.53%	1.91%
Expected dividend yield	—%	—%	—%
Weighted-average fair value per option	$5.62	$25.18	$14.01

Employee Stock Purchase Plan

	Years Ended December 31,		
	2016	2015	2014
Expected volatility	111.57%	57.77%	74.24%
Expected term (in years)	1.37	1.15	0.8
Weighted-average risk-free interest rate	0.75%	0.43%	0.09%
Expected dividend yield	—%	—%	—%
Weighted-average option value per share	$3.20	$22.10	$9.93

Utilization of Net Operating Loss Carryforwards

At December 31, 2016, we had net operating loss carryforwards for federal and state tax purposes of approximately $356.1 million and $287.2 million, respectively. At December 31, 2015, we had net operating loss carryforwards for federal and state tax purposes of approximately $296.6 million and $233.9 million, respectively. In addition, we had tax credit carryforwards for federal tax purposes of approximately $14.5 million as of December 31, 2016, 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 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, 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.

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RESULTS OF OPERATIONS

Comparison of the Years Ended December 31, 2016 and December 31, 2015

The following table summarizes our results of operations for the years ended December 31, 2016 and December 31, 2015, together with the changes in those items in dollars and percentage (in thousands, except percentages):

	Years Ended December 31,		Dollar Change Increase/(Decrease)	% Change
	2016	2015		
Revenues:				
Contract revenue	$5,702	$9,214	$(3,512)	(38.1)%
Collaboration and licensing revenue	—	1,548	(1,548)	(100.0)%
Total revenues	5,702	10,762	(5,060)	(47.0)%
Operating expenses:				
Research and development	58,647	97,717	(39,070)	(40.0)%
General and administrative	25,007	31,296	(6,289)	(20.1)%
Total operating expenses	83,654	129,013	(45,359)	(35.2)%
Loss from operations	(77,952)	(118,251)	40,299	(34.1)%
Other income (expense):				
Interest income (expense), net	1,562	879	683	77.7 %
Net loss	$(76,390)	$(117,372)	$40,982	(34.9)%

Contract Revenue

For the year ended December 31, 2016, contract revenue decreased to $5.7 million compared to $9.2 million for the year ended December 31, 2015. The decrease of $3.5 million, or 38.1%, was related to a decrease in reimbursable expenses related to our contract with BARDA.

Collaboration and Licensing Revenue

For the year ended December 31, 2016, we did not have any collaboration and licensing revenue. For the year ended December 31, 2015, total collaboration and licensing revenue was $1.5 million related to our collaboration and licensing agreement with ContraVir Pharmaceuticals.

Research and Development Expenses

For the year ended December 31, 2016, our research and development expenses decreased to $58.6 million compared to $97.7 million for the year ended December 31, 2015. The decrease of $39.1 million, or 40.0%, was primarily related to the following:

- a decrease of $31.0 million in oral BCV clinical expenses, comprised primarily of a decrease related to the completion of our Phase 3 SUPPRESS and AdVise clinical trials and the closeout of our SUSTAIN and SURPASS clinical trials;
- a decrease of $3.1 million in costs related to the development of oral BCV drug manufacturing, and
- a decrease in other research and development expenses, offset by
- increases in costs of approximately $3.6 million related to the development of an IV formulation of brincidofovir and development of CMX521, the company's asset for norovirus

General and Administrative Expenses

For the year ended December 31, 2016, our general and administrative expenses decreased to $25.0 million compared to $31.3 million for the year ended December 31, 2015. The decrease of $6.3 million, or 20.1%, was primarily related to the following:

- a decrease of $7.1 million as we delayed our commercialization readiness activities for brincidofovir;
- a decrease of $1.2 million in operational support costs as part of our cost-saving efforts; offset by
- a net increase in compensation and other employee related costs of $1.9 million, consisting of an increase of $1.7 million of share-based compensation and an increase of $0.2 million of compensation and benefits.

Interest Income (Expense), Net

For the year ended December 31, 2016, our interest income, net was $1.6 million compared to interest income, net of $0.9 million for the year ended December 31, 2015. The increase of $0.7 million was attributable to increased interest earned on higher cash and investment balances over prior year and a reduction in interest expense as our debt was paid in full in October 2015.

Comparison of the Years ended December 31, 2015 and December 31, 2014

The following table summarizes the results of our operations for the years ended December 31, 2015 and December 31, 2014, together with the year-over-year changes in those items in dollars (in thousands, except for percentages):

	Years Ended December 31,		Dollar Change Increase/(Decrease)	% Change
	2015	2014		
Revenues:				
Contract revenue	$9,214	$4,040	$5,174	128.1 %
Collaboration and licensing revenue	1,548	—	1,548	*
Total revenues	10,762	4,040	6,722	166.4 %
Operating expenses:				
Research and development	97,717	45,379	52,338	115.3 %
General and administrative	31,296	17,527	13,769	78.6 %
Total operating expenses	129,013	62,906	66,107	105.1 %
Loss from operations	(118,251)	(58,866)	(59,385)	100.9 %
Other income (expense):				
Interest income (expense), net	879	(446)	1,325	(297.1)%
Net loss	$(117,372)	$(59,312)	$(58,060)	97.9 %

* Not meaningful or not calculable

Contract Revenue

For the year ended December 31, 2015, contract revenue increased to $9.2 million compared to $4.0 million for the year ended December 31, 2014. The increase of $5.2 million, or 128.1%, was related to an increase in reimbursable expenses related to our contract with BARDA.

Collaboration and Licensing Revenue

For the year ended December 31, 2015, total collaboration and licensing revenue was $1.5 million. In December 2014, we entered into a collaboration and licensing agreement with ContraVir Pharmaceuticals. We recognized the upfront license fee payment as deferred revenue in 2014. During the second quarter of 2015, we completed our performance obligations related to this agreement and recognized $1.5 million of collaboration and licensing revenue. For the year ended December 31, 2014, we did not have any collaboration and licensing revenue.

Research and Development Expenses

For the year ended December 31, 2015, our research and development expenses increased to $97.7 million compared to $45.4 million for the year ended December 31, 2014. The increase of $52.3 million, or 115.3%, was primarily

related to the following:

- an increase in clinical trial expenses of $30.9 million primarily related to our Phase 3 SUPPRESS and AdVise studies, as well as the costs of initiating our Phase 3 SUSTAIN and SURPASS studies, which we have since closed;
- an increase in compensation and other employee related costs of $11.0 million, consisting of $6.5 million of compensation and benefit expense related to the addition of new employees to our clinical, regulatory, development and manufacturing departments and $4.5 million of share-based compensation;
- an increase in drug manufacturing costs of $5.7 million for raw materials as we began primary and secondary brincidofovir manufacturing campaigns;

- an increase of $2.9 million in legal and consulting expenses mainly related to the preparation of regulatory filings; and
- an increase in animal studies of $1.0 million related to work under the BARDA contract and other preclinical development expenses.

General and Administrative Expenses

For the year ended December 31, 2015, our general and administrative expenses increased to $31.3 million compared to $17.5 million for the year ended December 31, 2014. The increase of $13.8 million, or 78.6%, was primarily related to the following:

- an increase in compensation and other employee related costs of $5.9 million, consisting of an increase of $4.1 million of share-based compensation and $1.8 million of compensation and benefits related to the addition of new employees;
- an increase in other costs of $4.9 million as we expanded our commercialization preparations for brincidofovir; and
- an increase of $1.8 million in legal, accounting and consulting costs.

Interest Expense, Net

For the year ended December 31, 2015, our interest income, net was $0.9 million compared to interest expense, net of $0.4 million for the year ended December 31, 2014. The change of $1.3 million was attributable to increased interest earned on higher cash and investment balances over prior year and a reduction in interest expense as our debt was paid in full in October 2015.

LIQUIDITY AND CAPITAL RESOURCES

We have incurred losses since our inception in 2000 and, as of December 31, 2016, we had an accumulated deficit of $415.8 million. We anticipate that we will continue to incur losses for at least the next several years. In connection with the closing of our active clinical trials for brincidofovir, we have seen a reduction in expenses. However, we currently expect both research and development expenses and general and administrative expenses to trend upward modestly in 2017, and we will need additional capital to fund our operations, which we may obtain through one or more of equity offerings, debt financings, government or other third-party funding, strategic alliances and licensing or collaboration arrangements.

On May 27, 2014, we completed an underwritten public offering of 8,395,000 shares of common stock, including 1,095,000 shares sold pursuant to the full exercise of an option previously granted to the underwriters to purchase additional shares of common stock. All of the shares were offered by us at a price to the public of $14.22 per share. The net proceeds from this offering, after deducting underwriting discounts and commissions and other offering expenses payable by us, were approximately $111.8 million. The securities described above were offered by us pursuant to a shelf registration statement declared effective by the SEC on May 16, 2014. The shelf registration statement allows us to issue shares of our common stock and preferred stock, various series of debt securities and warrants to purchase any of such securities, up to a total aggregate offering price of $200.0 million from time to time in one or more offerings. As of December 31, 2016, we had sold approximately $119.4 million of our common stock under this shelf registration statement.

On November 5, 2014, we completed an underwritten public offering of 4,197,500 shares of common stock, including 547,500 shares sold pursuant to the full exercise of an option previously granted to the underwriters to purchase additional shares of common stock. All of the shares were offered by us at a price to the public of $29.00 per share. The net proceeds from this offering, after deducting underwriting discounts and commissions and other offering expenses payable by us, were approximately $114.0 million. The securities described above were offered by the

Company pursuant to an automatic shelf registration statement which immediately became effective by rule of the SEC on October 29, 2014.

On June 16, 2015, we completed an underwritten public offering of 4,341,250 shares of common stock, including 566,250 shares sold pursuant to the full exercise of an option granted to the underwriters to purchase additional shares of common stock. All of the shares were offered by us at a price to the public of $39.75 per share. The net proceeds from this offering, after deducting underwriting discounts and commissions and other offering expenses payable by us, were approximately $161.9 million. The securities described above were offered by us pursuant to an automatic shelf registration statement which immediately became effective by rule of the SEC on June 9, 2015.

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, short-term investments, and long-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, 2016, we have funded our operations principally with $595.5 million (net of issuance costs of $23.9 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, $51.7 million in revenue from our BARDA contract, debt financings totaling $21.0 million, $17.5 million of licensing revenue, and $13.3 million from stock option and warrant exercises and purchases under our Employee Stock Purchase Plan (ESPP). As of December 31, 2016, we had capital available to fund operations of approximately $278.1 million. Cash in excess of immediate requirements is invested in accordance with our investment policy, primarily with a view to liquidity and capital preservation.

During 2012, we entered into a loan and security agreement with SVB and MidCap allowing for borrowing up to $15 million. In January 2012, we borrowed $3 million under this agreement which had an interest only period for twelve months, followed by a thirty month principal and interest period at a rate of 8.25%. In September 2012, we borrowed an additional $12 million under this agreement which had an interest only period of six months, followed with a thirty-two month principal interest period at a rate of 8.25%. As of October 14, 2015, the principal balance of the loan was paid in full and no amounts remain outstanding.

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:	2016	2015	2014
Net cash used in operating activities	$(63,815)	$(99,708)	$(47,077)
Net cash provided by (used in) investing activities	94,065	(169,496)	(159,700)
Net cash provided by financing activities	608	161,347	225,263
Net increase (decrease) in cash and cash equivalents	$30,858	$(107,857)	$18,486

Operating Activities

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 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.

Net cash used in operating activities of $99.7 million for the year ended December 31, 2015 was primarily the result of our $117.4 million net loss, offset by the add-back of non-cash expenses of $13.0 million for stock based

compensation and $1.6 million of amortization of premiums on investments. The change in operating assets and liabilities includes an increase in accounts payable and accrued liabilities of $7.7 million primarily related to increased research and development activities for our Phase 3 SUPPRESS clinical trial, offset by an increase in prepaid expenses and other assets of $3.0 million and an increase of $2.4 million in accounts receivable due to an increase in reimbursable expenses related to our contract with BARDA.

Net cash used in operating activities of $47.1 million for the year ended December 31, 2014 was primarily the result of our $59.3 million net loss, offset by the add-back of non-cash expenses of $4.4 million for stock based compensation and $1.2 million of amortization of premiums on investments. The change in operating assets and liabilities includes an increase in accounts payable and accrued liabilities of $6.2 million primarily related to increased research and development activities for our Phase 3 SUPPRESS clinical trial, and a decrease of $0.1 million in accounts receivable due to a decrease in reimbursable expenses related to our contract with BARDA, offset by an increase in prepaid expenses and other assets of $0.1 million.

Investing Activities

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. Net cash used in investing activities of $169.5 million during the year ended December 31, 2015 was primarily the result of purchases of short-term and long-term investments, offset by sales and maturities of short-term and long-term investments. Net cash used in investing activities of $159.7 million during the year ended December 31, 2014 was primarily the result of purchases of short-term and long-term investments, offset by sales and maturities of short-term investments.

Financing Activities

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. Net cash provided by financing activities of $161.3 million for the year ended December 31, 2015 was primarily the result of approximately $161.9 million in net proceeds from the completion of a public offering and $4.2 million from the exercise of stock options, warrants and purchases under the ESPP, offset by $4.7 million in debt repayment and fees. Net cash provided by financing activities of $225.3 million for the year ended December 31, 2014 was primarily the result of approximately $225.9 million in net proceeds from the completion of two public offerings and $5.0 million from the exercise of stock options, warrants and purchases under the ESPP, offset by $5.7 million in debt repayment.

On May 27, 2014, we completed an underwritten public offering of 8,395,000 shares of common stock, including 1,095,000 shares sold pursuant to the full exercise of an option previously granted to the underwriters to purchase additional shares of common stock. All of the shares were offered by us at a price to the public of $14.22 per share. The net proceeds from this offering, after deducting underwriting discounts and commissions and other offering expenses payable by us, were approximately $111.8 million. The securities described above were offered by us pursuant to a shelf registration statement declared effective by the SEC on May 16, 2014. The shelf registration statement allows us to issue shares of our common stock and preferred stock, various series of debt securities and warrants to purchase any of such securities, up to a total aggregate offering price of $200.0 million from time to time in one or more offerings. As of December 31, 2016, we had sold approximately $119.4 million of our common stock under this shelf registration statement.

On November 5, 2014, we completed an underwritten public offering of 4,197,500 shares of common stock, including 547,500 shares sold pursuant to the full exercise of an option previously granted to the underwriters to purchase additional shares of common stock. All of the shares were offered by us at a price to the public of $29.00 per share. The net proceeds from this offering, after deducting underwriting discounts and commissions and other offering expenses payable by us, were approximately $114.0 million. The securities described above were offered by the Company pursuant to an automatic shelf registration statement which immediately became effective by rule of the SEC on October 29, 2014.

On June 16, 2015, we completed an underwritten public offering of 4,341,250 shares of common stock, including 566,250 shares sold pursuant to the full exercise of an option granted to the underwriters to purchase additional shares of common stock. All of the shares were offered by us at a price to the public of $39.75 per share. The net proceeds from this offering, after deducting underwriting discounts and commissions and other offering expenses payable by us, were approximately $161.9 million. The securities described above were offered by us pursuant to an automatic shelf registration statement which immediately became effective by rule of the SEC on June 9, 2015.

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. At present, we expect our research and development expenses and general and administrative expenses to trend upward modestly in 2017. 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 Study 999, 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 adenovirus 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, 2016 (in thousands):

	Total	Less Than 1 Year	1 – 3 Years	3 – 5 Years	More Than 5 Years
Operating leases (1)	$3,033	$ 826	$ 1,423	$ 784	$ —
Total	$3,033	$ 826	$ 1,423	$ 784	$ —

(1) Consists of our corporate headquarters lease encompassing 29,053 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 June 2018 and August 2018, 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. Under our license agreement with UC, we made milestone and sublicense payments totaling approximately $1.2 million through December 31, 2016. 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, 2016, 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 thousand 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, 2016 or 2015.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Shareholders of Chimerix, Inc.

We have audited the accompanying consolidated balance sheets of Chimerix, Inc. as of December 31, 2016 and 2015, and 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, 2016. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Chimerix, Inc. at December 31, 2016 and 2015, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2016, 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), Chimerix, Inc.'s internal control over financial reporting as of December 31, 2016, 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 2, 2017 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP
Raleigh, North Carolina
March 2, 2017

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Shareholders of Chimerix, Inc.

We have audited Chimerix, Inc.'s internal control over financial reporting as of December 31, 2016, 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). Chimerix, Inc.'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 Annual 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 conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). 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.

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.

In our opinion, Chimerix, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2016, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheets of Chimerix, Inc. as of December 31, 2016 and 2015, and 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, 2016 of Chimerix, Inc. and our report dated March 2, 2017 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP
Raleigh, North Carolina
March 2, 2017

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

	December 31,	
	2016	2015
ASSETS		
Current assets:		
Cash and cash equivalents	$51,463	$20,605
Short-term investments, available-for-sale	180,558	199,729
Accounts receivable	1,599	2,432
Prepaid expenses and other current assets	2,845	6,071
Total current assets	236,465	228,837
Long-term investments	47,407	124,040
Property and equipment, net of accumulated depreciation	2,843	3,045
Other long-term assets	55	70
Total assets	$286,770	$355,992
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$3,890	$10,458
Accrued liabilities	6,215	9,721
Total current liabilities	10,105	20,179
Lease-related obligations	441	354
Total liabilities	10,546	20,533
Stockholders’ equity:		
Preferred stock, $0.001 par value, 10,000,000 shares authorized at December 31, 2016 and 2015; no shares issued and outstanding as of December 31, 2016 and 2015	—	—
Common stock, $0.001 par value; 200,000,000 shares authorized at December 31, 2016 and 2015; 46,522,475 and 46,162,525 shares issued and outstanding at December 31, 2016 and 2015, respectively	46	46
Additional paid-in capital	692,422	675,591
Accumulated other comprehensive loss	(440)	(764)
Accumulated deficit	(415,804)	(339,414)
Total stockholders’ equity	276,224	335,459
Total liabilities and stockholders’ equity	$286,770	$355,992

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,		
	2016	2015	2014
Revenues:			
Contract revenue	$5,702	$9,214	$4,040
Collaboration and licensing revenue	—	1,548	—
Total revenues	5,702	10,762	4,040
Operating expenses:			
Research and development	58,647	97,717	45,379
General and administrative	25,007	31,296	17,527
Total operating expenses	83,654	129,013	62,906
Loss from operations	(77,952)	(118,251)	(58,866)
Other income (expense):			
Interest income (expense), net	1,562	879	(446)
Net loss	(76,390)	(117,372)	(59,312)
Other comprehensive loss:			
Unrealized gain (loss) on investments, net	324	(799)	35
Comprehensive loss	$(76,066)	$(118,171)	$(59,277)
Per share information:			
Net loss, basic and diluted	$(1.65)	$(2.67)	$(1.80)
Weighted-average shares outstanding, basic and diluted	46,267,064	43,878,326	33,003,714

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

CHIMERIX, INC.
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY (DEFICIT)
(in thousands, except share and per share data)

	Common Stock	Additional Paid-in Capital	Accumulated Other Comprehensive Gain (Loss)	Accumulated Deficit	Total Stockholders' Equity (Deficit)
Balance, December 31, 2013	$ 26	$ 261,243	$ —	$ (162,730)	$ 98,539
Share-based compensation	—	4,411	—	—	4,411
Exercise of stock options	2	4,591	—	—	4,593
Exercise of warrants	—	6	—	—	6
Employee stock purchase plan purchases	1	425	—	—	426
Issuance of 8,395,000 shares of common stock at $14.22 per share, net of issuance costs of $7,531	8	111,837	—	—	111,845
Issuance of 4,197,500 shares of common stock at $29.00 per share, net of issuance costs of $7,634	4	114,089	—	—	114,093
Comprehensive loss:					