

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

May 19, 2014

Date of Report (Date of earliest event reported)

Chimerix, Inc.

(Exact name of registrant as specified in its charter)

Delaware

(State or other jurisdiction
of incorporation)

001-35867

(Commission File Number)

33-0903395

(IRS Employer Identification No.)

**2505 Meridian Parkway, Suite 340
Durham, NC**

(Address of principal executive offices)

27713

(Zip Code)

Registrant's telephone number, including area code: (919) 806-1074

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligations of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

In this report, "Chimerix," "we," "us" and "our" refer to Chimerix, Inc.

Item 8.01 Other Events.

We are filing certain information for the purpose of updating aspects of the description of our business and expenses contained in our other filings with the Securities and Exchange Commission. A copy of this additional disclosure is attached as Exhibit 99.1 to this Form 8-K and is incorporated herein by reference.

Forward-Looking Statements

Statements contained in, or incorporated by reference into, this Current Report on Form 8-K regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Risks are described more fully in our filings with the Securities and Exchange Commission, including without limitation our most recent Quarterly Report on Form 10-Q and other documents subsequently filed with or furnished to the Securities and Exchange Commission. All forward-looking statements contained in this Current Report on Form 8-K speak only as of the date on which they were made. We undertake no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

<u>Exhibit No.</u>	<u>Description</u>
99.1	Additional Disclosure.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Chimerix, Inc.

Dated: May 19, 2014

By: /s/ Timothy W. Trost

Timothy W. Trost

Senior Vice President, Chief Financial Officer and Corporate Secretary

INDEX TO EXHIBITS

Exhibit No.	Description
99.1	Additional Disclosure.

2014 Research and Development Expenses

As previously announced, we plan to increase our research and development expenses for the foreseeable future as we continue development of brincidofovir for the prevention of cytomegalovirus (CMV) infection in hematopoietic cell transplant (HCT) recipients and for the treatment of adenovirus (AdV) infections, among other research and development activities. In particular, we expect our research and development expenses for 2014 to significantly exceed prior year levels beginning in the second quarter of 2014, as a result of:

- the timing of costs previously expected to occur in 2013 that will instead be incurred in 2014,
- the impact of SUPPRESS trial activities in 2014,
- the initiation of our pilot open-label study of brincidofovir for the treatment of AdV infections in March 2014, and
- the potential initiation of a planned pivotal Phase 3 study in the treatment of AdV infections later this year.

Assuming patient enrollment continues as we currently anticipate for SUPPRESS and our pilot open-label study of brincidofovir for AdV infections, and we initiate a pivotal Phase 3 study in adenovirus later this year as currently planned, our research and development expenses for the year ending December 31, 2014, may be as high as \$65.0 million. We are providing this forward-looking guidance with respect to 2014 research and development expenses solely in connection with the potential public offering of our common stock being announced concurrently with the filing of this Current Report on Form 8-K, and we do not expect to provide similar forward-looking guidance on a regular basis in the future.

Business Description

Chimerix Overview

Chimerix is a biopharmaceutical company dedicated to discovering, developing and commercializing novel, oral antivirals to address unmet medical needs. We were founded in 2000 based on the promise of our proprietary lipid technology to unlock the potential of some of the most broad-spectrum antivirals by enhancing their antiviral activity and safety profiles in convenient, orally administered dosing regimens. Our lead compound, brincidofovir (CMX001), is currently enrolling a Phase 3 clinical trial for the prevention of CMV and other viruses in HCT recipients, and in the pilot portion of a Phase 3 trial for the treatment of life threatening adenovirus infections. We anticipate completing enrollment in our Phase 3 CMV study in HCT by the end of 2014 and reporting data from this trial in mid-2015. We anticipate finalizing the Phase 3 protocol for the treatment of disseminated AdV infections in the second half of 2014 and initiating enrollment. In addition, we have an active discovery program leveraging our lipid technology and the Chimerix Chemical Library, both focusing on viral targets in areas of high unmet medical need.

Brincidofovir

CMV in HCT

More than 65% of HCT recipients are at increased risk of CMV reactivation due to prior exposure to CMV defined by evidence of antibodies to CMV in the blood (i.e., CMV seropositive). CMV, a human herpesvirus, is the most common infectious threat in HCT, with 80% of CMV-seropositive (R+) allogeneic transplant recipients developing detectable CMV in the blood, which is known to correlate with progression to disease and death, if untreated. Common manifestations of active CMV infection in immunosuppressed patients are pneumonia, gastrointestinal (GI) disease, hepatitis, and retinitis. In addition, because CMV itself is immunosuppressive, reactivation of the virus can predispose a patient to other opportunistic infections.

Rather than waiting for evidence of CMV disease, the most commonly accepted approach to avoid CMV is frequent monitoring for CMV in the blood and, if CMV replication is detected, initiation of anti-CMV preemptive therapy with intravenous ganciclovir or oral valganciclovir, available antivirals with the side-effect of suppression of neutrophils and an associated increased risk for bacterial and fungal infections.

The initial indication for which we are seeking regulatory approval for brincidofovir is prevention of CMV infection in recipients of allogeneic HCT who are seropositive for CMV. To the extent that the risk-benefit ratio for brincidofovir is established in SUPPRESS, particularly in prevention of clinical manifestations of other dsDNA viral infections, indications in patient populations with more moderate CMV risk estimates may be pursued. Based on a survey of recent literature, we believe that the following table reflects the risk of CMV reactivation in HCT patients:

Risk Assessment for CMV Reactivation in HCT

Type	CMV Serostatus	Risk of CMV Infection ⁽¹⁾	Non-Relapse Mortality ⁽²⁾
Allogeneic	R+	80%	21%
	D-/R-	3%	17%
	D+/R-	30%	18%
Autologous	R+	40%	27%

(1) "R+" refers to recipient seropositive for CMV, "R-" refers to recipient seronegative for CMV, "D+" refers to donor seropositive for CMV, and "D-" refers to donor seronegative for CMV.
(2) "Risk of CMV Infection" is defined as the likelihood of detectable CMV in blood.
(3) "Non-Relapse Mortality" is defined as death in the first year following HCT that is not due to relapse of the underlying disease.

According to the Center for International Blood and Marrow Transplant Research and the Organ Procurement and Transplantation Network, more than 20,000 HCTs and 28,000 SOTs are performed annually in the United States, with similar numbers of transplants performed annually in Europe according to the European Group for Blood and Marrow Transplantation and the World Health Organization. More than 65% of HCT recipients are at increased risk of CMV infection due to prior exposure to CMV defined by evidence of antibodies to CMV in the blood (i.e., CMV seropositivity).

HCT remains underutilized, with many patients referred for a transplant only when they reach an advanced stage of disease. In order to increase the number of patients who could potentially benefit from HCT, there has been significant focus on alternative stem cell sources such as unrelated donors and umbilical cord blood stem cells. However, use of unrelated donors for stem cell results in higher risk of reactivation of dsDNA viruses such as CMV.

Overall, the number of stem cell transplants being performed in the United States has grown at approximately 4% annually since 2000. Of the allogeneic transplants, the unrelated donor subset has been growing at a higher rate than other subsets within HCT.

Phase 3 SUPPRESS Trial

Brincidofovir is an investigational oral nucleotide analog that has shown broad-spectrum antiviral activity against all five families of DNA viruses that affect humans. We initiated the Phase 3 SUPPRESS trial of brincidofovir in the third quarter of 2013. The trial is designed to demonstrate the safety and efficacy of brincidofovir in the prevention of CMV infection through the first 24 weeks following a HCT and, if successful, will serve as the basis for Accelerated Approval for brincidofovir.

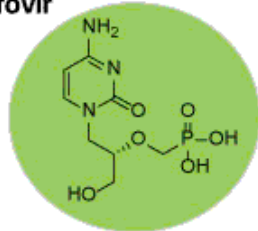
SUPPRESS is enrolling 450 allogeneic (non-self) HCT recipients who are at high risk of CMV infection in the post-transplant period based on antibody evidence of a prior infection with CMV, referred to as "CMV seropositive" or "recipient (R+) seropositive." Because there is no approved CMV prevention available for these patients, the control or "placebo" arm of the study is the currently accepted standard of intensive monitoring for evidence of CMV reactivation in the blood and, if CMV replication is detected, initiation of early or "preemptive" antiviral therapy. Subjects are randomized 2-to-1 to the active brincidofovir arm (n=300) or the standard-of-care/placebo arm (n=150). Dosing of brincidofovir or placebo begins as soon after the transplant as the patient can swallow a tablet, generally within the first two weeks, and continues through Week 14, the period of greatest risk for viral infections. Subjects will be followed in the trial for an additional 10 weeks after the last dose of study drug, for a total of 24 weeks after transplant. The Roche TAQMAN® real-time PCR assay, which was recently approved by the FDA, will be used to monitor levels of CMV in the blood. The trial is powered (greater than 85%) to detect a relative 50% decrease in clinically significant CMV infection in subjects receiving brincidofovir versus those receiving placebo. Secondary endpoints include evidence of other dsDNA viruses, including AdV, VZV, BKV, and other herpesviruses such as HHV-6, which contribute to morbidity and mortality in the first year following HCT.

We anticipate completing enrollment for the SUPPRESS trial in late 2014 and reporting data in mid-2015.

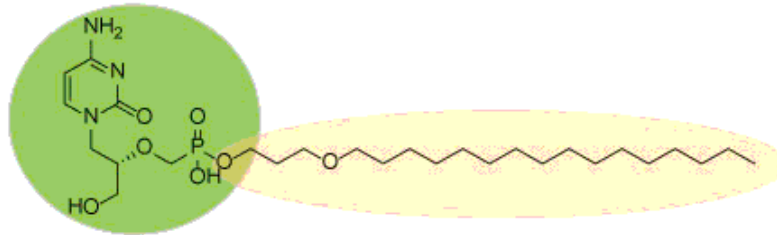
Background on Brincidofovir

Brincidofovir is a broad-spectrum antiviral currently in Phase 3 clinical development for CMV prevention in adult HCT recipients. Utilizing our proprietary lipid technology, this nucleotide compound is dosed orally in tablet or liquid form. Brincidofovir's safety and tolerability profile supports its continued investigation as a potential antiviral prevention for multiple dsDNA viruses. The structures of cidofovir and brincidofovir are graphically depicted below.

Cidofovir



Brincidofovir (CMX001)

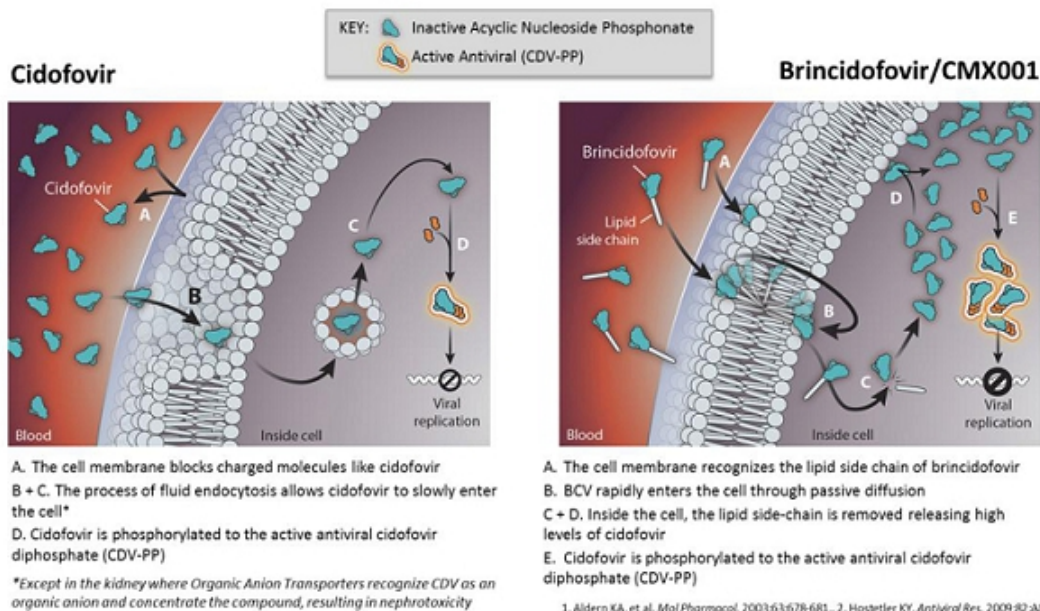


Our proprietary technology results in higher intracellular levels of the active antiviral CDV-PP, while avoiding bone marrow toxicities and cidofovir-related kidney and toxicity. As a result of its phospholipid structure, brincidofovir remains intact in the plasma, is cleaved to cidofovir only after entering cells, and is then converted to CDV-PP, the active antiviral. By more efficiently delivering drug inside cells, our technology allows for more cidofovir to be delivered to the site of viral replication while minimizing the amount of free cidofovir in the plasma, which in turn decreases the risk of nephrotoxicity.

Additionally, dosing with brincidofovir results in levels of CDV-PP detectable in the cells for a long period of time. This allows for less frequent dosing and a low pill burden, potentially important benefits for patients.

Brincidofovir's broad-spectrum potency against dsDNA viruses has been characterized *in vitro* in cell culture systems and *in vivo* in multiple animal models. In cell culture assays, brincidofovir is typically 50- to 100-fold more potent than cidofovir against dsDNA viruses, including herpesviruses, adenoviruses, polyomaviruses, papillomaviruses, and orthopoxviruses.

The graphic below demonstrates the relative plasma and the intracellular concentrations for each compound, as well as the intracellular activation and site of action of brincidofovir versus cidofovir.



The following table shows the concentrations of brincidofovir and each of the approved and investigational antivirals required to reduce viral replication by 50% *in vitro*. Smaller numbers depict a more potent molecule than larger numbers, and results depicted by “>” in general are above a threshold that would indicate antiviral activity (i.e., adequate *in vitro* data do not exist to support pursuing a clinical indication). Data are compiled from multiple sources and include multiple materials and methodologies; comparisons should be limited to general trends in orders of magnitude differences in *in vitro* potency.

Broad Spectrum Activity of Brincidofovir versus Approved and Investigational Antivirals (EC₅₀ in μM)

Viral Family	Virus	Brincidofovir (CMX001) EC ₅₀ (μM)	Cidofovir EC ₅₀ (μM)	Ganciclovir ⁽¹⁾ EC ₅₀ (μM)	Foscarnet EC ₅₀ (μM)	Acyclovir EC ₅₀ (μM)	Maribavir EC ₅₀ (μM)	Letermovir EC ₅₀ (μM)
Herpes	Cytomegalovirus (CMV)	0.001	0.4	3.8	50-800	> 200	0.31	0.005
	Epstein-Barr Virus (EBV)	0.03	65.6	0.9	< 500	6.2	0.63	>10
	Human Herpesvirus 6A (HHV-6A)	0.003	2.7	5.8	16	10	Inactive	> 10
	Human Herpesvirus 8 (HHV-8)	0.02	2.6	8.9	177	> 100	Inactive	No data
	Herpes Simplex Virus 1 (HSV-1)	0.01	3.0	0.7	92-95	3.8	Inactive	> 10
	Herpes Simplex Virus 2 (HSV-2)	0.02	6.5	2.5	91-96	4.4	Inactive	> 10
	Varicella Zoster Virus (VZV)	0.0004	0.5	1.3	39.8	3.6	Inactive	> 10
Adenovirus	Adenovirus 7 (AdV7)	0.02	1.3	4.5-33	Inactive (AdV2)	> 100	No data	> 10 (AdV2)
Polyoma	BK Virus (BKV)	0.13	115	> 200	Inactive	> 200	No data	No data
	JC Virus (JCV)	0.045	> 0.1	No data	Inactive	No data	No data	No data
Papilloma	Human Papillomavirus 11 (HPV-11)	17	716	Inactive	No data	Inactive	No data	No data
Pox	Variola	0.1	27	No data	No data	No data	No data	No data
	Vaccinia	0.8	46	> 392	Inactive	> 144	No data	No data

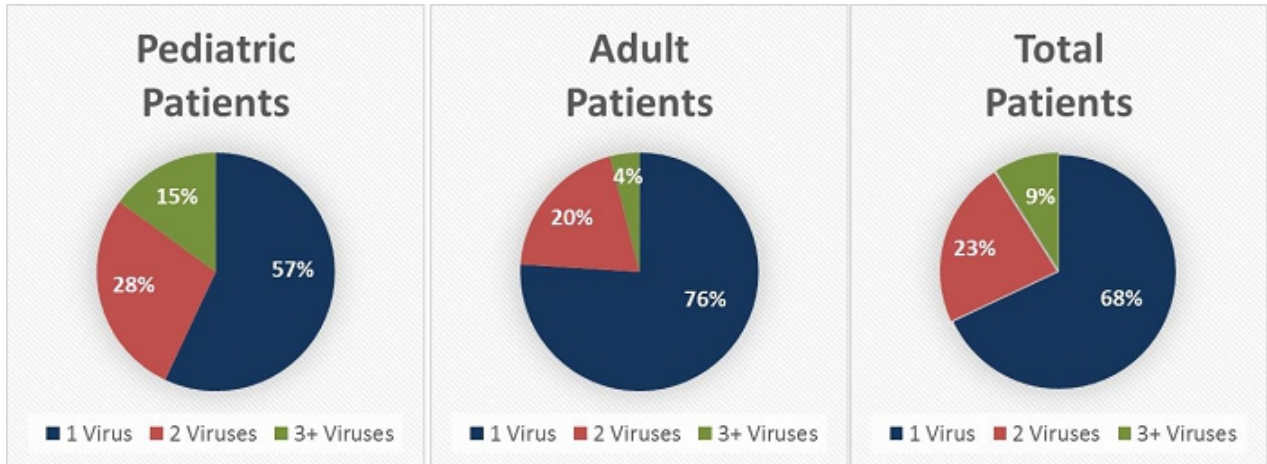
(1) Valganciclovir is rapidly converted to ganciclovir *in vivo*. Accordingly, ganciclovir is the relevant compound for cell activity studies.

Although brincidofovir delivers the same active antiviral, CDV-PP, as intravenous cidofovir, the ability of brincidofovir to deliver CDV intracellularly through the lipid-conjugate technology results in brincidofovir demonstrating approximately 800-fold improvement *in vitro* in activity against BKV, more than 400-fold more activity against CMV, 65-fold more activity against AdV and 250-fold more activity against variola major, the causative agent of smallpox.

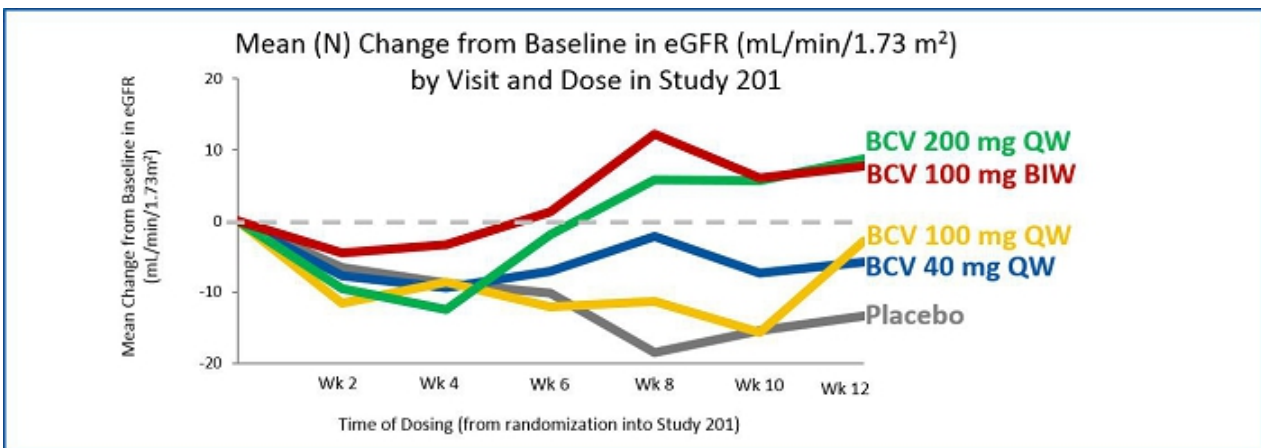
Brincidofovir has a high barrier to CMV resistance, and no mutations shown to have phenotypic resistance to any anti-CMV antiviral were detected in Study 201. *In vitro* brincidofovir-resistant CMV is slow to emerge, involves a unique mutation, and has reduced fitness compared to wild-type CMV. We have completed a 39-week chronic toxicology study in monkeys and 26-additional studies in mice, rabbits, rats, dogs, and monkeys. Based on results from these studies, we do not currently plan to conduct additional toxicology studies. We have also completed 41 Absorption, Distribution, Metabolism and Excretion (ADME) studies which demonstrate that brincidofovir is readily absorbed and widely distributed after oral administration in animals. *In vitro* cytochrome P450 and drug transporter inhibition studies indicated low-to-moderate potential for drug-drug interactions. In the development of Vistide®, Gilead identified mammary rat tumors that led to the inclusion of potential carcinogenicity in a black box warning. We observed similar findings with brincidofovir and may have a black box warning for brincidofovir with regard to carcinogenic risk.

Because HCT recipients are also at increased risk for other DNA viral infections including HHV-6, Epstein-Barr Virus (EBV), AdV and BK virus (BKV), key secondary endpoints in SUPPRESS include clinical events associated with these viruses such as encephalitis, respiratory infections, graft failure and measures of kidney function. Data collected in our previous studies with brincidofovir indicate that immunosuppressed patients are at risk of additional, non-CMV viral infections as per the below.

Immunosuppressed Patients are at Risk for Multiple Viral Infections



In Study 201, CMV (R+) patients assessed for BKV at enrollment: 41% in the placebo arm (n=59) and 45% of brincidofovir patients (n=171) were BKV+ in urine. See “—Successful Identification of Brincidofovir Dose in Study 201” below. Data from Study 201 suggests that BCV may mitigate the effect of BKV infection on renal function and hematuria post-HCT, as measured by changes in estimated glomerular filtration rate (eGFR) as seen in the graph below.



Baseline GFR	Week 2	Week 4	Week 6	Week 8	Week 10	Post-Week 1
Placebo	-7 (56)	-9 (46)	-10 (35)	-19 (36)	-15 (21)	-13 (57)
Brincidofovir 100 mg BIW	-5 (49)	-3 (44)	1 (33)	12 (31)	6 (21)	8 (49)

p=0.0013
p=0.0103
p=0.0025

During the first year following allogeneic HCT, the rate of non-relapse mortality (mortality not related to recurrence of the underlying malignancy) is approximately 20%, with perhaps one-third of these deaths attributable to the direct and indirect effects of CMV and other DNA viruses. We hope to show that by preventing the significant morbidity related to DNA viruses, we can positively impact the overall success of allogeneic transplantation in the patients who are undergoing this potentially life-saving procedure.

Through decreasing the proportion of subjects with CMV reactivation, brincidofovir may impact both direct effects of CMV such as CMV pneumonitis or hepatitis, and may also reduce the indirect effects of CMV reactivation including inflammation and immune suppression which lead to bacterial, fungal, protozoal and other viral opportunistic infections. It may also be possible to decrease the use of currently available anti-CMV drugs known to have specific toxicities such as neutropenia that increase the risk of bacterial and fungal infections. Another key set of data being collected in SUPPRESS are healthcare utilization costs, including the costs of the toxicities associated with the currently available antivirals, which we believe will be instrumental in future formulary and pricing discussions.

Successful Identification of Brincidofovir Dose in Study 201

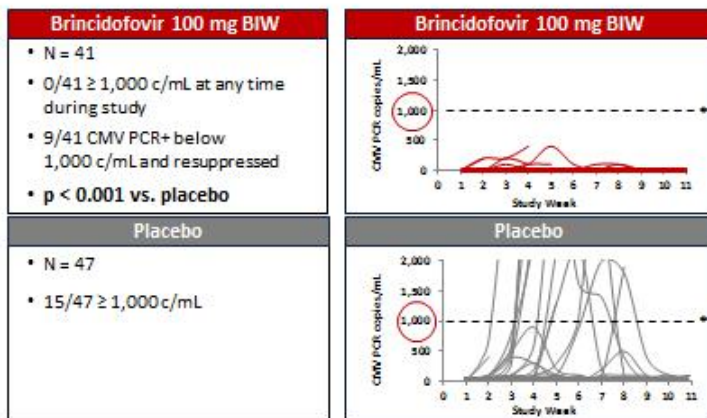
The SUPPRESS study design and patient population substantially mirrors that of our Phase 2 dose-escalation study, Study 201, the results of which were published in September 2013 in the New England Journal of Medicine (N Engl J Med 2013;369:1227-36). In Study 201, a statistically significant decrease in CMV reactivation (CMV PCR > 200 c/mL at the time of the last dose of study drug) was demonstrated for brincidofovir 100 mg BIW versus placebo (p = 0.002).

Study 201 was a randomized, placebo-controlled, dose-escalation study in CMV seropositive (R+) allogeneic HCT recipients, including higher risk patients who received HLA mismatched and cord blood source HCT, as well as those who have undergone ex vivo T-cell depletion, evaluating the ability of brincidofovir to prevent CMV infection. Subjects in five dosing groups received either placebo or oral brincidofovir, in doses ranging from 40 mg once weekly to 200 mg BIW. The primary endpoint was defined as (i) the incidence of CMV disease at any time during therapy, or (ii) a CMV polymerase chain reaction (PCR) assay result of greater than 200 copies/mL at the time of the last dose of study drug. All subjects who received at least one dose of drug or placebo and had at least one efficacy evaluation post baseline were included in the primary analysis, regardless of their CMV PCR status (negative or positive) at baseline (modified intent to treat, or mITT, population).

All brincidofovir doses and dose regimens in Study 201 demonstrated antiviral activity when compared to placebo, with the exception of the lowest dose, 40 mg QW. The proportion of subjects who developed CMV disease or a CMV PCR positive result at the end of 100 mg BIW dosing period was 10% (five of 50 subjects) versus 37% (22 of 59 subjects) for placebo-treated subjects (p=0.002, mITT population).

In a pre-specified subgroup analysis of subjects who were CMV negative at baseline, zero of 41 subjects (0%) in the brincidofovir 100 mg BIW group developed CMV PCR of 1,000 copies/mL or more during the brincidofovir dosing period, compared to 15 of 47 (32%) of subjects in the placebo cohort (p<0.001) (see figures below).

Brincidofovir Demonstrated Dose-Associated CMV Suppression in Phase 2



*Represents clinically relevant threshold for CMV assay.
 Subjects CMV negative at Baseline.
 Source: *N Engl J Med* 2013; 369:1227-36

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There was no indication of myelotoxicity or nephrotoxicity associated with brincidofovir at any dose in the Phase 2 Study, nor discontinuations from the study related to these events. Based on the decreased CMV events in both BIW dosing cohorts, and the superior tolerability of the 100 mg BIW dose in Study 201, brincidofovir 100 mg BIW was felt to demonstrate the most favorable risk benefit ratio and was selected for further evaluation.

Because of the severity of their underlying illnesses and the multiple drugs administered to HCT patients both pre- and post-transplant, there is a high background level of adverse events (AEs) in this patient population. Of the AEs reported in Study 201 in 20% or more of subjects, GI-associated events (including diarrhea, nausea, vomiting and abdominal pain) and elevated ALT levels generally increased in frequency with increasing doses of brincidofovir.

In the cohort of subjects receiving the highest dose of brincidofovir explored in Study 201, brincidofovir 200 mg BIW, an increased rate of GI AEs was reported, particularly diarrhea. Diarrhea in the transplant setting has the potential to originate from a variety of sources, including conditioning regimens, concomitant medications, and infections. At this time, the FDA requested that doses of brincidofovir be limited to a total weekly dose of 200 mg or less. As part of the FDA's request, we implemented a program-wide Safety Monitoring and Management Plan (SMMP) that included interruption of study drug for subjects who experienced Grade 3 or higher GI AEs. In the final cohort of subjects in our Phase 2 study, 10% of the subjects administered brincidofovir 100 mg BIW discontinued brincidofovir due to GI AEs, compared to 3% in the placebo group. A decrease in serum albumin from baseline was found to provide an additional marker for discriminating drug-related diarrhea from diarrhea of other etiologies. We believe that monitoring of serum albumin concentrations coupled with dose interruption is an appropriate strategy to decrease the severity of GI AEs without loss of antiviral activity and could allow for completion of the intended therapy duration. Following the introduction of the SMMP in Study 202 for AdV, less than 10% of subjects discontinued from brincidofovir BIW or QW due to GI AEs. The SMMP is included in the ongoing Phase 3 SUPPRESS study.

A dose-related, transient increase in ALT was associated with brincidofovir therapy. At a dose of 100 mg BIW, approximately 30% of subjects experienced ALT increases greater than three times the upper limit of normal, compared to 16% in the placebo group. When present, the ALT increases follow a predictable pattern and return to baseline levels following completion of therapy. The brincidofovir-related increases in ALT were not associated with increases in aspartate aminotransferase (AST) or bilirubin. Few clinical hepatobiliary AEs were reported in association with brincidofovir therapy and most were mild or moderate in intensity. The ALT increases observed in Study 201 were consistent with ALT elevations observed across all preclinical species exposed to brincidofovir, a finding considered non-adverse as there was no histopathologic evidence of liver injury or hepatic necrosis. In Study 202, there were no Grade 3/4 elevations of ALT in either brincidofovir dosing cohort, and no temporary or permanent discontinuations for ALT elevations.

There has been no evidence of nephrotoxicity with brincidofovir preclinically. The mechanism of nephrotoxicity for intravenous cidofovir is directly related to its status as a dianion at physiologic pH, and the high plasma concentrations of intravenous cidofovir needed to reach therapeutic intracellular levels of CDV-PP. Cidofovir is rapidly taken up by cells in the kidney by a receptor called the human organic anion transporter one (hOAT-1), which leads to high concentrations of cidofovir in the proximal renal tubules in the kidneys and subsequent renal toxicity. Brincidofovir is a dianion and thus not a substrate for hOAT-1.

The lack of nephrotoxicity observed with brincidofovir in preclinical in vitro and animal studies is supported by clinical data. Based on the pharmacokinetic and safety data generated in our Compassionate Use Program, the FDA granted a waiver for the conduct of a renal insufficiency clinical pharmacology study. A further indication of brincidofovir’s lack of nephrotoxicity was observed in Study 201, where there was a dose-related improvement in estimated GFR in the subjects receiving therapeutic doses (100 mg BIW or 200 mg QW), and a more significant difference for those subjects found to be shedding BKV in the urine and receiving brincidofovir as compared with subjects on placebo. These data provide a clinical correlate to the in vitro activity of brincidofovir against BKV.

Comparison of SUPPRESS to Study 201

Although SUPPRESS is similar in the population targeted for enrollment (CMV seropositive allogeneic HCT recipients) and the duration of therapy (through to approximately day 100 after transplant), one significant change in design from Study 201 to SUPPRESS is the initiation of dosing prior to engraftment (evidence of a functioning bone marrow), a change that could positively impact the probability of success of SUPPRESS. In Study 201, as in similar studies in CMV prevention using other antiviral agents, dosing began only after evidence of engraftment in order to avoid known or potential hematologic toxicities. Review of the hematologic safety data from brincidofovir’s safety database of over 900 individuals exposed to date provided evidence of a the lack of hematologic toxicity or myelotoxicity, and resulted in the ability to begin dosing of brincidofovir in SUPPRESS in the first days following HCT, prior to engraftment. The ability to dose in the very early post-transplant period may further decrease rates of CMV infection based on recently published data regarding the reactivation of latent CMV in the early post-transplant period. In addition, dosing in the early post-transplant period may increase the likelihood that brincidofovir may prevent reactivation of other DNA viruses such as BKV and HHV-6 which can reactivate in the first weeks after transplant.

Additional differences in design between Study 201 and SUPPRESS are summarized in the table below.

	Phase 2 Study (CMX001-201)	Phase 3 Study (SUPPRESS) (CMX001-301)
Population	N=230; CMV Ab+ (R+)	N=450; CMV Ab+ (R+)
Inclusion Criteria	Adult, high risk allogeneic HCT; CMV PCR + allowed	Adult, high risk allogeneic HCT; CMV PCR - only
Dosing Regimen	Dose Ranging	100 mg BIW
Dosing Initiation	After engraftment	As early as patient can swallow tablet
Efficacy Primary Endpoint	CMV Viremia at time of last study drug dose	CMV viremia per protocol requiring preemptive therapy through Wk 24
Safety	BCV dosed fasted; dose interruption SMMP for GI AEs in final cohort	BCV dosed with food; SMMP allows dose interruption, modification, or reduction for GI AEs

The risk benefit ratio for medications intended for prevention of infection requires a higher standard of safety and tolerability than medications intended for the treatment of established infection, based on the expectation that a larger number of individuals will receive the medication for prevention in order to avoid clinically significant disease (e.g., the number needed to treat to avoid a single infection). With respect to brincidofovir, the safety and tolerability that has been established to date support its continued development as an effective prevention of CMV and other DNA viruses. With regards to the safety and tolerability concerns specific to the HCT population, the lack of observed hematological or bone marrow toxicity is a critical determinant of brincidofovir's use in this population. By contrast, ganciclovir/valganciclovir's negative effects on survival of the graft, the primary objective of transplant hematologists, represents the primary limitation of the use of those drugs. Furthermore, we believe brincidofovir may have the potential to improve graft survival due to brincidofovir's activity against dsDNA viruses that are known to result in graft failure. As shown on the table below, a combined analysis of data from previous studies with placebo-controlled brincidofovir are consistent with this hypothesis.

	Studies 201/202		Study 350	
Clinical Graft Failure	BCV	Placebo	BCV	BCV + (v)GCV
Baseline ANC <1500	0 / 25	1 / 16 (6.3%)	2 / 33 (6.1%)	2 / 8 (25.0%)
All Subjects	2 / 112 (1.8%)	3 / 69 (4.3%)	2 / 119 (1.7%)	2 / 28 (7.1%)

Brincidofovir has demonstrated a lack of toxicity for the kidney. In Study 201, monitoring for potential renal toxicity included regular serum creatinine levels, calculation of glomerular filtration rate (GFR), and monitoring for the presence of blood in the urine. Subjects receiving one of the effective doses of brincidofovir had a dose-related improvement in kidney function which was consistent and statistically significant across all three measures, while patients who received placebo had a decline through the duration of dosing and the first week of follow-up. In preclinical assessments, brincidofovir has been shown to be an inefficient substrate for hOAT-1, the transporter associated with renal dysfunction and renal failure following the intravenous administration of cidofovir (Vistide®).

In Study 201, the most significant baseline predictor that correlated with improvements in renal function was evidence of infection with BK virus, a DNA virus which is a member of the polyomavirus family. This is the first evidence of a potential clinical effect of brincidofovir on manifestations of BKV in HCT recipients. While this potential positive effect may be significant for HCT recipients, it could be even more important in kidney transplant recipients, where BKV has been associated with loss of function and loss of the kidney graft. The evaluation of brincidofovir in kidney transplant recipients is currently being considered in our clinical development plans.

In Study 201, gastrointestinal adverse events and diarrhea in particular were confirmed as the dose-limiting toxicity of brincidofovir. An SMMP was implemented to identify potentially drug-related diarrhea and other gastrointestinal events and to allow a temporary dose interruption. Earlier identification of potentially drug-related GI symptoms and temporary dose interruptions has allowed study subjects to restart brincidofovir successfully in a majority of cases. The SMMP was included in the Phase 2 study in patients with AdV infection (Study 202), with one of 30 patients in the brincidofovir cohorts permanently discontinuing brincidofovir due to diarrhea. The SMMP has been included in the ongoing Phase 3 study of brincidofovir for the prevention of CMV in HCT recipients, SUPPRESS. The SMMP also includes early identification and dose-interruption for potentially drug-related elevations in the liver enzyme ALT, which are reversible upon dosing cessation and typically not accompanied by increases in bilirubin. In our preclinical and early clinical studies, a proportion of individuals had evidence of low-grade ALT increases. In preclinical studies these ALT elevations were not accompanied by any evidence of histopathology and were considered non-adverse.

Regulatory Strategy for Brincidofovir and the Prevention of CMV

If brincidofovir obtains regulatory approval, we believe the most likely first approved indication for use for brincidofovir will be for the prevention of CMV in high risk (e.g., CMV seropositive) allogeneic HCT recipients. We intend to seek approval of such an indication in the United States by means of an accelerated approval based on the use of a "surrogate endpoint," namely, CMV detected in the plasma at a level which results in the initiation of preemptive therapy for CMV infection. If we are successful in obtaining accelerated approval for use of brincidofovir for such indication, we believe the following are the three primary means by which we might obtain a traditional approval for that indication:

- agreement with the FDA, supported by a public meeting, that CMV viremia be accepted as a validated “surrogate endpoint” for CMV pivotal studies;
- conduct of a second, confirmatory clinical trial which correlates CMV viremia with clinical endpoints (for example, a CMV prevention trial in recipients of solid-organs); or
- if SUPPRESS were to reach statistical significance on mortality or graft survival.

Adenovirus Study 304

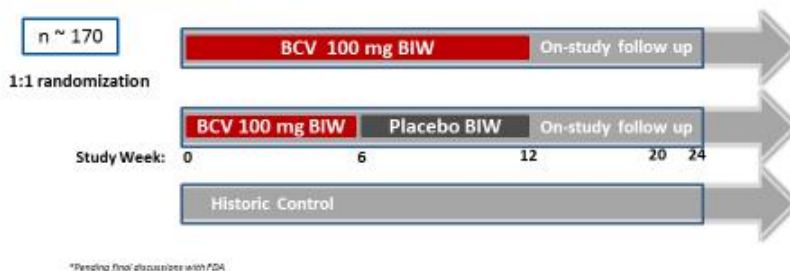
In March 2014, we initiated a pilot study of brincidofovir for the treatment of AdV infections in immunocompromised pediatric and adult patients. The study is currently enrolling the “pilot” portion, data from which will inform the final study design for Study 304. There is no minimum or maximum patient number requirement for this pilot portion. We have reached a general agreement with the FDA regarding the design of a Phase 3 study that would include patients similar to those participating in this pilot study, and which could provide data to support the marketing application of brincidofovir for treatment of disseminated adenovirus infections. We believe an indication for the treatment of AdV has the potential to support traditional approval in the U.S. based on clinical endpoints.

Below is a possible design of a Phase 3 AdV trial. Design of the Phase 3 AdV trial remains subject to discussion with the FDA. There can be no assurance that we will reach agreement with the FDA on a final trial design on a timely basis or at all, or that any final trial design we do reach agreement on with the FDA will not vary from the possible design shown below.

Phase 3 Proposed AdV Trial In Planning Stage

Populations:

- **Cohort A** - Allogeneic HCT recipients with localized or asymptomatic AdV infection
- **Cohort B** - Allogeneic HCT recipients with disseminated AdV disease
- **Cohort C** - Autologous HCT, Solid Organ Transplants, other Immunocompromised
- **Cohorts A and B Randomized and Blinded**
- **Proposed Primary endpoint:** AdV disease-free survival at Week 20
- **Design:** 6 week vs. 12 week dosing duration
- **Dosing:** Twice-weekly (BIW) for 6 or 12 weeks
- **Timeline:** Final protocol second half of 2014



Phase 3 Solid Organ Transplant Trial

We are actively exploring the conduct of a potential Phase 3 clinical trial studying the effectiveness of brincidofovir in high risk kidney transplant recipients (CMV seropositive donor, seronegative recipient (D+/R-)). The final study design remains in active discussions with the FDA and European regulators.

Pediatric Indication for Brincidofovir

We plan to submit an application for a pediatric indication for the use of brincidofovir in addition to our adult HCT indication application. In connection with any such application, we will need to conduct a study to provide confirmatory pharmacokinetic and safety data for a new pediatric commercial formulation. Depending on the final design and timing of Study 304, we may be able to obtain such data through Study 304.

Potential Exploration of Brincidofovir in other viral indications

In light of the broad spectrum activity observed *in vitro*, brincidofovir could potentially be explored for benefit in the following diseases related to DNA viruses:

Potential Exploration of BCV in Other Viral Indications

dsDNA Virus	Disease
HPV	Recurrent Respiratory Papillomatosis (RRP)
CMV	Glioblastoma
EBV/HHV-6	DRESS Syndrome
EBV	Post Transplant Lymphoproliferative Disorder (PTLD)
HSV	Encephalitis in neonates & adults Acyclovir resistance in HIV+ individuals
JCV	Progressive Multifocal Leukoencephalopathy (PML)
VZV	Herpes Zoster (shingles)
HPV	Adjuvant to cancer therapy

Potential collaborative Study: Glioblastoma and CMV

We are examining the potential use of brincidofovir for the treatment of glioblastoma, a tumor of the brain or spinal cord. Published reports have posited a relationship between tumor formation and CMV infection, including one exploratory study investigating the use of valganciclovir in patients with Grade 4 glioblastoma that demonstrated a potential survival benefit.

Our Chemical Library and Lipid Technology

Lipid-Antiviral-Conjugate Technology

Our proprietary technology, which we refer to as lipid-antiviral-conjugate technology, is used to covalently modify a drug molecule with a lipid side chain that mimics the phospholipid component of cellular membranes. The lipid mimetic can then utilize natural uptake pathways to achieve oral bioavailability, enhance uptake into cells, avoid many toxicities, and yield higher intracellular concentrations of active antivirals.

We believe that our lipid-antiviral-conjugate technology can be used to develop new drugs from parent molecules having a known mechanism of action but with an improved safety and efficacy profile relative to the parent. Preclinical studies and in vitro experiments on a number of drugs have shown specific improvements in biological activity compared with the parent drug.

The primary example of our proprietary lipid technology is brincidofovir, which was developed to deliver a potent but relatively toxic drug, cidofovir, into cells. Use of cidofovir has been limited by significant toxicities, particularly kidney toxicity. The lipid-bearing brincidofovir molecule allows delivery of a potent but less toxic molecule than the unmodified cidofovir parent molecule. Thus brincidofovir has a higher benefit risk ratio that allows its use in the setting of prevention of CMV disease and potentially 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 that are candidates for lipid conjugation. We have an active discovery program focusing on viral diseases where there is significant unmet medical need. We are currently screening the library for activity against more than thirty viruses including flaviviruses, influenza, herpesviruses and polyomaviruses. Lead chemical series have been identified for CMV and BK viruses and novel compounds with promising activity are being evaluated in various pre-clinical testing models. We believe that several compounds active against key pathogens are amenable to enhancement using our proprietary lipid technology.

Our Strategy

Our strategy is to discover, develop and commercialize novel oral antiviral 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. We are also weighing the potential of developing brincidofovir for use in non-transplant settings, in light of the broad-spectrum anti-viral activity against numerous DNA viruses.

The key components of our strategy are:

- **Pursue multiple indications for which brincidofovir could receive approval.**
 - o *Prevention of CMV in High Risk HCT Recipients.* During 2013, we began enrollment of SUPPRESS, our Phase 3 clinical trial of brincidofovir for the prevention of CMV in HCT recipients. The SUPPRESS study design and population largely resembles our Phase 2 dose-ranging CMV prevention study (Study 201).
 - § If successful, the data from SUPPRESS will be used to support our application for accelerated approval of brincidofovir for the prevention of CMV in HCT recipients. We anticipate completing enrollment for the SUPPRESS trial in late 2014 and reporting data in mid-2015. If approved, we believe that we are well positioned to maximize the commercial potential of brincidofovir as there are currently no approved therapies for prevention of CMV reactivation in HCT. We are in discussions with the FDA regarding the study design for our confirmatory Phase 3 study for traditional approval of brincidofovir for the prevention of CMV. The confirmatory study could be conducted in kidney transplant recipients.
 - § During 2014, we plan to expand our activities to Europe. We anticipate adding several sites to the SUPPRESS trial. We are also in the process of obtaining scientific advice from the European Medicines Authority on our brincidofovir development plan.
 - o *Treatment of Life-Threatening AdV Infections in Immunocompromised Patients.* In March 2014, we initiated a pilot open-label study of brincidofovir for the treatment of AdV infections in immunocompromised pediatric and adult patients. The study is currently enrolling the “pilot” portion, data from which will inform the final study design for Study 304. We are in general agreement with the FDA regarding the design of a Phase 3 study that would include patients similar to those participating in this pilot trial and which could provide data to support the marketing application of brincidofovir for treatment of disseminated adenovirus infections. However, design of the Phase 3 study remains subject to discussions with the FDA.
 - o *Prevention of CMV in SOT Recipients.* We intend to conduct a Phase 3 clinical trial studying the effectiveness of brincidofovir in high risk recipients of kidney transplant (CMV seropositive donor, seronegative recipient (D+/R-)). In SOT recipients, CMV infection generally occurs after discontinuation of the currently available antivirals.
 - **Evaluate Additional Patient Populations and Applications for Use of Brincidofovir.** In addition to our initial development program focusing on CMV in transplant recipients, we are evaluating other patient populations and applications for potential future treatment opportunities with brincidofovir.
 - o *Additional patient populations.* We intend to evaluate brincidofovir in other immunocompromised patient populations. Beyond the transplant population, patients are susceptible to multiple DNA viral diseases due to congenital or induced immune deficiencies secondary to biologics therapy for autoimmune and other disorders. Through our Expanded Access Program, hundreds of patients have received brincidofovir for the treatment of a variety of viral diseases.
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- o *Additional viral indications.* Brincidofovir has shown activity in vitro against the five families of DNA viruses that cause disease in humans. In addition to the development progression for the prevention of CMV, we have also evaluated brincidofovir for use in patients with AdV infection. In an exploratory Phase 2 study in patients with AdV infection, brincidofovir consistently suppressed AdV viremia and showed a favorable numeric difference for progression to AdV disease and non-relapse mortality.

§ We also continue to work with BARDA to develop brincidofovir as a medical countermeasure for the treatment of variola virus, the DNA virus responsible for smallpox. In March 2014, we presented data demonstrating that rabbits receiving three doses of brincidofovir experienced a statistically significant survival benefit over placebo when infected with rabbitpox. We intend to evaluate brincidofovir for the treatment of patients with various other DNA virus induced diseases. This process has begun with the collection of secondary endpoint data in our SUPPRESS trial and may continue with more virus-specific clinical trials in the future.

Discover and Develop Additional Product Candidates to Strengthen our Antiviral Product Portfolio. We have an active discovery and preclinical development program focused on identifying and developing new compounds that can be used to treat viral diseases for which no current therapeutic option exists or in areas of high unmet medical need. Current examples include influenza and norovirus. We intend to leverage our knowledge and experience of nucleosides to advance compounds in the Chimerix Chemical Library through Investigational New Drug (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 technology to significantly improve the drug profile of molecules with limitations in safety or delivery.

Commercial Agreements

BARDA

In February 2011, we entered into a contract with BARDA for the advanced development of CMX001 as a medical countermeasure in the event of a smallpox release (Contract Number HHSO100201100013C). 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 CMX001 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 of around one year each, 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 completed the base performance segment of the contract on May 31, 2013 and are currently working under the first option segment of the contract which has been extended and is currently scheduled to end August 31, 2014. BARDA must notify us at least 30 days before the end of the first option segment if it intends to exercise the second option segment of the contract. If all option segments are exercised by BARDA, the term of the contract would be extended to February 15, 2016. As of March 31, 2014, we had recognized revenue in aggregate of \$33.5 million with respect to the base performance segment and the first extension period.

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.

We anticipate renegotiating certain aspects of the smallpox animal plan to take into account recent guidance from the FDA for development of CMX001 under the Animal Efficacy Rule. The results of this negotiation are uncertain and we do not anticipate continuing this program without ongoing support from BARDA.

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. 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, 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, 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. Specifically, the license agreement contains a due diligence requirement stating that we must commence a Phase III clinical trial for the first Licensed Product within 9 years of the Effective Date (as those terms are defined within the license agreement). On January 31, 2011 we received a letter from UC stating that we had satisfied these requirements, thereby waiving compliance with further due diligence obligations.

Merck

In July 2012, we entered into a collaboration and license agreement granting Merck exclusive worldwide rights to CMX157, our novel nucleoside phosphonate being developed for the treatment of HIV infection. Under the terms of the agreement, Merck received an exclusive worldwide license for any human use of CMX157 and agreed to use commercially reasonable efforts to develop and commercialize CMX157 in the United States and at least three major European markets. Following execution of the agreement, we received a \$17.5 million upfront payment from Merck.

On May 14, 2014, we received notice from Merck of their intent to terminate the collaboration and exclusive license agreement with Chimerix. Pursuant to the agreement, the termination will be effective 90 days after receipt of the notification. As a consequence of the termination, all license rights previously granted to Merck under the collaboration and exclusive license agreement will revert to Chimerix. The compound is currently being evaluated for future development opportunities, however, Chimerix has no present plans for allocation of current or future resources to the development of CMX157.

Commercial Operations

In anticipation of potential regulatory approval and commercial launch of brincidofovir, we are building out select commercial functions in the U.S. tied to key milestones, such as availability of topline data from the SUPPRESS trial in mid-2015, and the potential filing of the NDA for brincidofovir.

Patients who receive HCT and solid organ transplants (SOTs) are likely to be treated at a small number of major medical centers by specialized teams of physicians. There are approximately 200 U.S. transplant centers, which overlap in performing HCT and SOT. The management of therapies for transplant patients is largely the responsibility of transplant physicians and infectious disease specialists who oversee post-transplant therapies. Overall, transplant and transplant infectious disease treatment is a small clinical discipline with a clearly identified group of key opinion leaders (KOLs). While the standard of care for post-transplant therapies may vary by institution and country, it is often driven by research activities or publications of these KOLs from academic transplant research centers. Many of these key opinion leaders have participated in our clinical trials and/or have experience using brincidofovir through our Compassionate Use Program. We believe we can access these KOLs to help inform future commercialization plans for brincidofovir, including the prioritization and probability of success in evaluating additional study populations involving DNA viruses.

If approved for the prevention of CMV in patients who have received a HCT, we believe it is possible for us to commercialize brincidofovir for this indication in the United States and Canada with a relatively small commercial infrastructure, which may include a contract sales force, partner sales force, or internal team. While our commercialization efforts would initially be focused on physicians who are responsible for HCT recipients, this commercial infrastructure would serve as the foundation for an expanded focus on physicians who are responsible for SOT recipients, subject to market approval in this patient population.

Outside of the United States and Canada, subject to obtaining necessary marketing approvals, we likely will 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 collaborators, depending on, among other things, the applicable indications, the related development costs, and our available resources.

Competition

Our industry is highly competitive and subject to rapid and significant technological change. While we believe that our experience and scientific and commercial knowledge provide us with competitive advantages, we may face competition from large and small pharmaceutical and biotechnology companies, including specialty pharmaceutical and generic drug companies, academic institutions, government agencies, research institutions and others.

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 reduced or eliminated if our competitors develop or market products or other novel technologies that are more effective, safer 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 may be affected by the availability of generic products.

We expect that, 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 the prevention of CMV in allogeneic stem cell transplant patients. Potentially competing products that are currently marketed include:

- oral and intravenous ganciclovir, a drug that is sold by generic manufacturers;
 - Valcyte® (valganciclovir), a prodrug of ganciclovir that is marketed by Hoffmann-La Roche Inc.;
 - Cytogam®, a pooled CMV hyperimmunoglobulin, marketed by CSL Limited;
 - Vistide® (cidofovir for injection), marketed by Gilead Sciences, Inc.; and
 - Foscavir® (foscarnet sodium for injection), marketed by Clinigen Group plc and generic manufacturers.
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We are aware of several product candidates currently in development that 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 pursuant to an exclusive worldwide license agreement between AiCuris GmbH & Co. KG and Merck; and
- ASP0113 (TransVax), a CMV prevention vaccine, licensed to Astellas Pharma Inc. from Vical Incorporated and in development by Astellas and Vical.

Additional vaccine products are being developed by GlaxoSmithKline plc (GlaxoSmithKline), Novartis International AG, sanofi-aventis U.S. (Sanofi), and a variety of university and governmental organizations. Other products used against the same viruses targeted by brincidofovir include valacyclovir, an antiviral drug marketed by GlaxoSmithKline and a number of generic manufacturers; leflunomide, a drug approved for rheumatoid arthritis and sold in the United States by Sanofi under the brand name Arava®; and quinolone antibiotics, which are manufactured by a variety of branded pharmaceutical companies and generic manufacturers. Furthermore, we anticipate that we will face intense and increasing competition as new products enter the market, as advanced technologies become available and as generic forms of currently branded products become available.

Finally, the development of new treatment methods for the diseases we are targeting could render our product candidates non-competitive or obsolete. 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 placed to establish market share if we obtain the required regulatory approvals for brincidofovir. However, even with those benefits, we may not be able to make promotional claims that brincidofovir is superior to these competing products, and brincidofovir may be unable to compete successfully against these products. See “Part II Item 1A. Risk Factors—Risks Related to Commercialization of Our Product Candidates” in our Quarterly Report on Form 10-Q for the period ended March 31, 2014.

Our Intellectual Property

We strive to protect and enhance the proprietary technologies that we believe are important to our business, and seek to obtain and maintain 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 are not currently aware of any third-party patents (other than patents we have licensed) encompassing our proprietary compounds brincidofovir.

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 our licenses to use intellectual property owned by third parties, preserve the confidentiality of our trade secrets and operate without infringing the valid and enforceable patents and other proprietary rights of third parties. We also rely on know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen, and maintain our proprietary position in the field of nucleoside phosphonates.

We believe that we have a strong intellectual property position and substantial know-how relating to the development and commercialization of our lipid-antiviral conjugates, including brincidofovir and derivatives of brincidofovir consisting of patents or patent applications that we own or have in-licensed from third parties. We cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our technology.

Our objective is to continue to expand our intellectual property estate by filing patent applications directed to dosage forms, methods of treatment, and identification of additional nucleoside phosphonate compounds and their derivatives, in order to protect our lipid-antiviral conjugate therapeutics and to maintain our position in the antiviral field. Specifically, we seek patent protection in the United States and in certain other jurisdictions for novel compositions of matter covering brincidofovir, and chemistries which facilitate the synthesis of nucleoside phosphonate compounds, including brincidofovir, as well as uses of these compounds in a variety of anti-viral therapies, where available and when appropriate. Our policy is to pursue, maintain, and defend patent rights, whether developed internally or licensed from third parties, and to protect the technology, inventions, and improvements that are commercially important to the development of our business. We are also expanding our intellectual property estate into the area of novel antifungal nucleoside phosphonates.

Brincidofovir

The patent portfolio for brincidofovir is directed to cover compositions of matter (including polymorphs), formulation, manufacturing methods of polymorphic forms, and methods of use. This patent portfolio includes issued U.S. patents, pending U.S. patent applications, and corresponding foreign national and regional counterpart patents and patent applications. The patents and patent applications relating to brincidofovir include patents and patent applications owned by us, as well as patents and patent applications in-licensed (exclusive license) patent from The Regents of the University of California. The issued composition of matter patents in-licensed from the Regents of the University of California (U.S. Patent Nos. 6,716,825; 7,034,014; 7,094,772; and 7,790,703), if the appropriate maintenance, renewal, annuity, and other government fees are paid, are expected to expire in 2020. The issued composition of matter (polymorphic form) owned by Chimerix, Inc. (U.S. Patent No. 8,569,321), if the appropriate maintenance, renewal, annuity, and other government fees are paid, is expected to expire in 2031. The issued methods of use patents in-licensed from the Regents of the University of California (U.S. Patent Nos. 6,716,825; 7,452,898; and 7,790,703), if the appropriate maintenance, renewal, annuity, and other government fees are paid, are expected to expire in 2020. The issued methods of use patents owned by Chimerix, Inc. (U.S. Patent Nos. 8,642,577 and 8,614,200), if the appropriate maintenance, renewal, annuity, and other government fees are paid, are expected to expire in 2029 and 2030; respectively. Based on our current development plan, we believe that an additional term of up to five years for one of the brincidofovir U.S. patents may result from the patent term extension provision of the Hatch-Waxman Amendments of 1984 (the Hatch-Waxman Act). We expect that the remaining patent applications in this portfolio, if issued, and if appropriate maintenance, renewal, annuity, and other governmental fees are paid, would expire between 2020 and 2033, excluding any additional term from patent term adjustment or patent term extension. Assuming one of the U.S. composition of matter or method of use patents covering brincidofovir were awarded the maximum patent term extension, the term of that patent could extend to December 2025. The patent term calculation method and the provisions under the Hatch-Waxman Act are described under “— Patent Term” below.

The term of issued brincidofovir composition of matter patents in other jurisdictions (Australia, Canada, Europe, Hong Kong, India, Japan, Mexico, Russia, and South Africa) and methods of use patents and patent applications (if applicable) relating to brincidofovir (in Australia, Canada, China, Europe, Hong Kong, India, Japan, Mexico, Russia, and South Africa), if the appropriate maintenance, renewal, annuity, and other government fees are paid, are expected to expire between 2020 and 2031. These patents and patent applications (if applicable), depending on the national laws, may benefit from extension of patent term in individual countries. In the European Union member countries, for example, a supplementary protection certificate (SPC), if obtained, provides a maximum five years of market exclusivity. The duration of the SPC can be extended to five and a half years when the SPC relates to a human medicinal product for which data from clinical trials conducted in accordance with an agreed Pediatric Investigation Plan (PIP) have been submitted. Likewise, in Japan, the term of a patent may be extended by a maximum of five years in certain circumstances.

CMX157

The patent portfolio for CMX157 is directed to cover compositions of matter, formulation, and methods of use. This patent portfolio includes issued U.S. patents, pending U.S. patent applications, and corresponding foreign national and regional counterpart patents and patent applications. The patents and patent applications relating to CMX157 include patent applications owned by us, as well as patents and patent applications in-licensed (exclusive license) from The Regents of the University of California. The issued composition of matter patents (U.S. Patent Nos. 6,716,825; 7,034,014; 7,094,772; 7,790,703; 7,687,480 and 8,710,030), if the appropriate maintenance, renewal, annuity, and other government fees are paid, are expected to expire in 2020. The issued methods of use patents (U.S. Patent Nos. 6,716,825; 7,790,703; and 7,687,480), if the appropriate maintenance, renewal, annuity, and other government fees are paid, are expected to expire in 2020. We believe that an additional term of up to five years for one of the CMX157 U.S. patents may result from the patent term extension provision of the Hatch-Waxman Act. We expect that the patent applications in this portfolio, if issued, and if appropriate maintenance, renewal, annuity, and other governmental fees are paid, would expire between 2020 and 2033, excluding any additional term from patent term adjustment or patent term extension. The patent term calculation method and the provisions under the Hatch-Waxman Act are described under “—Patent Term” below.

The term of issued CMX157 composition of matter patents in other jurisdictions (Australia, Canada, Europe, Hong Kong, India, Japan, Mexico, Russia, and South Africa) and methods of use patents and patent applications (if applicable) relating to CMX157 (in Australia, Canada, China, Europe, Hong Kong, India, Japan, Mexico, Russia, and South Africa), if the appropriate maintenance, renewal, annuity, and other government fees are paid, are expected to expire between 2020 and 2031. Like the patents relating to brincidofovir, the patents and patent applications (if applicable), covering CMX157, depending on the national laws, may also benefit from extension of patent term in individual countries.

Other Product Candidates

In addition to brincidofovir, we have a chemical library of more than 10,000 heterocyclic compounds purchased from the University of Michigan which includes approximately 3,500 nucleoside analog candidates for lipid conjugation. We also license certain intellectual property rights relating to these compounds from the University of Michigan, in exchange for which we agree, among other things, to use commercially reasonable efforts to develop and commercialize products utilizing the licensed intellectual property, and to pay certain royalties and other fees to the University of Michigan. Focused screening of the library has identified viable hits against multiple pathogens including compounds with activity against influenza and compounds with activity against both CMV and BKV. Lead selection is in progress for a dual active CMV/BKV programs. We believe additional nucleoside phosphonate antiviral compounds, unrelated to brincidofovir, are protected under U.S. Patents 7,994,143; 7,749,983; 8,008,308; and 8,309,565, which are expected to expire between 2020 and 2028, if the appropriate maintenance, renewal, annuity, and other government fees are paid.

Patent Term

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 antiviral platform and 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 Chimerix as a whole.

The term of individual patents and patent applications listed in previous sections will depend upon the legal term of the patents in the countries in which they are obtained. In most countries, the patent term is 20 years from the date of filing of the patent application (or parent application, if applicable). For example, if an international (PCT) application is filed, any patent issuing from the PCT application in a specific country expires 20 years from the filing date of the PCT application. In the United States, however, if a patent was in force on June 8, 1995, or issued on an application that was filed before June 8, 1995, that patent will have a term that is the greater of twenty years from the filing date or seventeen years from the date of issue.

Under the Hatch-Waxman Act, the term of a patent that covers an FDA-approved drug may also be eligible for patent term extension (PTE). PTE permits patent term restoration of a U.S. patent as compensation for the patent term lost during the FDA regulatory review process. The Hatch-Waxman Act permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug is under regulatory review. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended. Further, certain new drug applications may obtain an additional six months of marketing exclusivity if the drug manufacturer submits certain FDA-requested information relating to the use of the active moiety in a pediatric population (pediatric exclusivity). Similar patent term extension provisions may be available in Europe and certain other foreign jurisdictions to extend the term of a patent that covers an approved drug. When possible, depending upon the length of clinical trials and other factors involved in the filing of a new drug application (NDA) we expect to apply for patent term extensions for patents covering nucleoside phosphonates and their derivatives, and their use in treating various diseases. As a specific example, if we are awarded the maximum length of PTE, our U.S. granted composition of matter patents relating to brincidofovir would have an expected expiration date of December 20, 2025. However, depending on any changes in our clinical path, the PTE may not be granted, or may be less than the maximum.

For additional information on patent term extension and the BPCA, see “—Government Regulation and Product Approval” below.

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 product that will be used in clinical trials of brincidofovir. 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 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 and a contract manufacturer for the drug substance. We have validated the drug substance production process for brincidofovir at a scale of up to 100 kilograms, which is an amount that safely exceeds our currently projected commercial requirements. We have completed transferring the drug substance manufacturing process to our selected contractor that will produce the commercial supply of drug substance and drug product. 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 and a separate firm as the supplier of drug product. 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 and suspension) are also manufactured under contract. We have validated manufacturing of brincidofovir tablets at a 165 kg commercial scale. In addition, stability data are available to support sufficient commercial shelf life. We have also developed a suspension formulation for brincidofovir and have manufactured that formulation at pilot scale. We are currently evaluating manufacturers to optimize tablet and suspension formulation production to meet forecasted commercial demand.

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.

Government Regulation and Product Approval

Government authorities in the United States, at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, 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 before it may be legally marketed in the United States and by the appropriate foreign regulatory agency before it may be legally marketed in foreign countries.

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, approval process or after 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 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 an 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 audit 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 volunteers or 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. 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 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 by three months if the FDA requests or the NDA sponsor otherwise provides additional information or clarification regarding information already provided in the submission within the last three months before the PDUFA goal date.

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 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. Orphan drug status in the European Union has similar but not identical benefits to those provided in the United States.

Expedited Development and Review Programs

The FDA has a Fast Track program that is intended to expedite or facilitate the process for reviewing new drugs and biological products that meet certain criteria. Specifically, new drugs and biological products are eligible for Fast Track 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. Unique to a Fast Track product, 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 a Fast Track program, 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-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product. Fast Track designation, priority review and accelerated approval do not change the standards for approval but may expedite the development or approval process.

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 payors include government health programs such as Medicare and Medicaid, managed care providers, private health insurers and other organizations. These third-party payors 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 payors. 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 payors 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 payors.

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 payors, 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 payors 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 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 European Union 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 European Union 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 much like the IND prior to the commencement of human clinical trials. In the European Union, 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, clinical trial development 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 European Union 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 that required in the European Union, with the exception of, among other things, country-specific document requirements.

For other countries outside of the European Union, 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 March 31, 2014, we had 55 full-time employees. Of these employees, 41 employees are engaged in research and development activities and 14 employees are engaged in 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 340, Durham, North Carolina 27713 in a facility we lease encompassing approximately 14,500 square feet of office space. The leases for this facility expire in February 2015 and 2018. We separately lease an additional 4,600 square feet of laboratory space in Durham, North Carolina. The lease for this facility expires in June 2014.

Our corporate website address is www.chimerix.com. The information contained on, or that can be accessed through, our website is not part of this Current Report on Form 8-K, and the inclusion of our website address in this Current Report on Form 8-K is an inactive textual reference only.
