UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the Fiscal Year Ended December 31, 2019

Or

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from_____to

Commission File Number: 001-37609

MYOKARDIA, INC.

(Exact name of registrant as specified in its charter)

Delaware	**2834**	**44-5500552**
(State or other jurisdiction of incorporation or organization)	**(Primary Standard Industrial Classification Code Number)**	**(I.R.S. Employer Identification No.)**

1000 Sierra Point Parkway

Brisbane, CA 94005

(Address of Principal Executive Offices) (Zip Code)

(650) 741-0900

(Registrant's Telephone Number, Including Area Code)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading symbol(s)	Name of each exchange on which registered
Common Stock	MYOK	NASDAQ Global Select Market

Securities registered pursuant to Section 12(g) of the Act:

None

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

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

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

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☒	Accelerated filer	☐
Non-accelerated filer	☐	Smaller reporting company	☐
		Emerging growth company	☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes ☐ No ☒

The aggregate market value of the common stock held by non-affiliates of the registrant was approximately $2,271,068,236 as of June 28, 2019 based upon the closing sale price on the NASDAQ Global Select Market reported for such date. Shares of common stock held by each executive officer and director and certain holders of more than 10% of the outstanding shares of the registrant's common stock have been excluded in that such persons may be deemed to be affiliates of the registrant. Shares of common stock held by other persons, including certain other holders of more than 10% of the outstanding shares of common stock, have not been excluded in that such persons are not deemed to be affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

The number of outstanding shares of the registrant's common stock on February 24, 2020 was 46,574,538 shares.

DOCUMENTS INCORPORATED BY REFERENCE

Part III of this Annual Report on Form 10-K incorporates information by reference to portions of the definitive proxy statement for the registrant's 2020 Annual Meeting of Stockholders, to be filed within 120 days of the registrant's fiscal year ended December 31, 2019.

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Annual Report on Form 10-K for the Fiscal Year Ended December 31, 2019

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends affecting the financial condition of our business. Forward-looking statements should not be read as a guarantee of future performance or results and will not necessarily be accurate indications of the times at, or by, which such performance or results will be achieved. Forward-looking statements are based on information available at the time those statements are made and/or management's good faith belief as of that time with respect to future events and are subject to risks and uncertainties that could cause actual performance or results to differ materially from those expressed in or suggested by the forward-looking statements.

Forward-looking statements include all statements that are not historical facts. In some cases, you can identify forward-looking statements by terms such as "may," "might," "will," "objective," "intend," "should," "could," "can," "would," "expect," "believe," "anticipate," "project," "target," "design," "estimate," "predict," "potential," "plan" or the negative of these terms, and similar expressions intended to identify forward-looking statements, and similar expressions and comparable terminology intended to identify forward-looking statements. These statements reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties, including those set forth below in Item 1A, "Risk Factors" and elsewhere in this Annual Report on Form 10-K. Forward-looking statements include, but are not limited to, statements about:

- Timing of and ability to generate positive data from our clinical trials of mavacamten, danicamtiv (formerly MYK-491), MYK-224, and any other drug candidate we may pursue;
- our ability to enroll patients in our clinical trials at the pace that we project;
- our reliance on third parties to conduct our clinical trials and to manufacture drug product for use in our clinical trials;
- our ability to execute our clinical development plans and obtain regulatory approval for any of our product candidates without the need for large, outcome-based studies;
- our ability to identify and advance through clinical development any additional product candidates from our precision medicine platform;
- our ability to obtain and maintain intellectual property protection for our precision medicine platform and our product candidates;
- our ability to successfully build a specialty sales force and commercial infrastructure to market mavacamten and any other product candidates from our programs;
- our ability to compete with companies currently producing or engaged in the clinical development of treatments for the disease indications that we pursue;
- our expectations as to the extent to which we will be able to commercialize mavacamten and any of our other products that are approved;
- the rate and degree of market acceptance of our products in the future;
- our expectations regarding government and third-party payor coverage and reimbursement;
- developments and projections relating to our competitors or our industry;
- our expectations as to our ability to successfully establish and successfully maintain appropriate relationships with potential collaboration partners and derive significant value from those collaborations;
- our financial performance including estimates of our expenses, ongoing losses, capital requirements, future revenue and our needs for or ability to obtain additional financing; and
- other risk factors described in Item 1A under the caption "Risk Factors."

Given these uncertainties, you should not place undue reliance on these forward-looking statements. These forward-looking statements represent our estimates and assumptions only as of the date of this Annual Report on Form 10-K and, except as required by law, we undertake no obligation to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise after the date of this Annual Report on Form 10 -K. We qualify all of our forward-looking statements by these cautionary statements.

All brand names or trademarks appearing in this report are the property of their respective holders. Unless the context requires otherwise, references in this report to "MyoKardia," the "Company," "we," "us," and "our" refer to MyoKardia, Inc. and its wholly-owned subsidiaries.

PART I

ITEM 1. BUSINESS

Overview

We are a clinical-stage biopharmaceutical company pioneering a precision medicine approach to discover, develop and commercialize targeted therapies for the treatment of serious cardiovascular diseases. Precision medicine involves discovering and developing therapies that target the biological basis of disease for patient populations whose condition is defined by shared underlying defects and/or disease characteristics. By targeting the biomechanical defects underlying a given condition, we believe our therapeutic candidates can correct or offset the downstream disruption in cardiac muscle function that drives disease progression.

Since our inception in 2012, we have generated a robust pipeline of small molecules that target diseases of the heart muscle, or cardiomyopathies. Our initial research has focused on genetic mutations in sarcomeric proteins of the heart muscle. These mutations directly affect the power of contraction, the rate of relaxation, or both, reducing the overall ability of the heart to pump blood at an output that matches the needs of the rest of the body. Our lead therapeutic candidate, mavacamten, is an orally administered allosteric modulator of cardiac myosin being developed for the treatment of hypertrophic cardiomyopathy (HCM). HCM is the most common heritable cardiomyopathy, estimated to affect one in every 500 people worldwide. Mavacamten is intended to reduce cardiac muscle contractility and enhance diastolic relaxation by inhibiting the excessive myosin-actin cross-bridge formation that underlies the excessive contractility, left ventricular hypertrophy and reduced compliance which are characteristic of HCM.

Mavacamten is initially being developed to address the obstructive form of the disease, which accounts for approximately two-thirds of the HCM patient population. Data from our pivotal Phase 3 EXPLORER-HCM clinical trial of approximately 250 patients with obstructive HCM are anticipated in the second quarter of 2020. Pending the outcome of the EXPLORER-HCM study, we plan to file a New Drug Application (NDA) with the U.S. Food and Drug Administration (FDA) seeking regulatory approval of mavacamten for the treatment of symptomatic obstructive HCM.

Based on evidence generated from clinical and preclinical studies, we tested mavacamten in our Phase 2 MAVERICK-HCM study, which enrolled patients with the non-obstructive form of HCM to more directly assess mavacamten's impact on diastolic dysfunction. This study was completed in November of 2019; results have provided a basis for advancing mavacamten into a planned Phase 2 clinical trial in a targeted population of heart failure patients whose disease is characterized by diastolic dysfunction, commonly referred to as heart failure with preserved ejection fraction (HFpEF). MAVERICK-HCM data also support the advancement of mavacamten into late-stage studies of non-obstructive HCM patients. We plan to present and/or publish complete results from the MAVERICK-HCM study in the first quarter of 2020. We are also seeking to review the data generated to date in the non-obstructive HCM population with the FDA and obtain input on future study design in this indication.

Patients who complete either the EXPLORER-HCM or MAVERICK-HCM studies are eligible to enroll in a MAVA long-term extension (LTE) study of mavacamten (MAVA-LTE). In addition, we continue to follow patients from our Phase 2 PIONEER-HCM study in the PIONEER-OLE open-label extension study. In addition, we expect to initiate a new clinical trial (VALOR-HCM) by mid-2020, to assess whether treatment with mavacamten may obviate the need for invasive septal reduction procedures.

In addition to mavacamten, we have generated the following programs to address a variety of disruptions in heart muscle contraction and filling:

- Danicamtiv (formally MYK-491) is our orally-administered small molecule designed to increase cardiac contractility without impairing diastolic filling in patients with systolic heart failure, commonly referred to as heart failure with reduced ejection fraction, or HFrEF. We are initially developing danicamtiv for patients with dilated cardiomyopathy (DCM) and have completed Phase 1 and Phase 2a safety studies. Our next study of danicamtiv will be Phase 2 study in patients with genetically driven DCM caused by mutations of the sarcomere which we plan to initiate in the second quarter of 2020.
- MYK-224 is our second small molecule program for the treatment of HCM targeting hypercontractility and impaired relaxation. MYK-224 is currently in a Phase 1 trial in healthy adults, for which topline results are expected in the third quarter of 2020. Pending these data, we anticipate advancing MYK-224 into a Phase 2 clinical trial before year-end 2020.
- ACT-1 is directed toward increasing cardiac contractility in certain forms of genetic dilated cardiomyopathy, or DCM. ACT-1 has a distinct mechanism from danicamtiv and is in preclinical development.
- LUS-1 is intended to counteract muscle abnormalities that result in impaired relaxation of the left ventricle, without decreasing contractility for certain cardiomyopathy or HFpEF patient populations. LUS-1 is currently advancing through preclinical development.

We have discovered all of the compounds in our pipeline internally and retain global development and commercialization rights to all of our programs. We believe consolidated control over our entire portfolio will allow us to make strategic decisions about how we advance each of our therapeutic candidates in alignment with our precision medicine approach.

Our Strategy

We are pioneering a precision medicine approach to the discovery and development of targeted cardiovascular disease therapeutics. Our strategy for success in this area includes three core tenets:

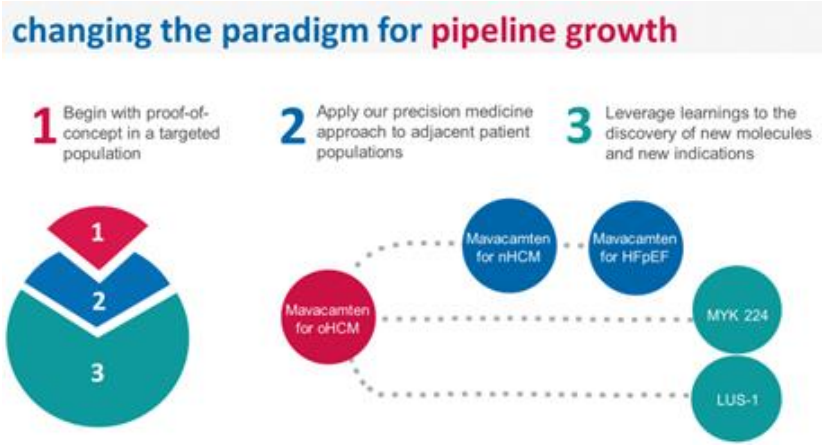
1) **Apply a precision medicine approach to cardiovascular disease drug discovery, development and commercialization.** We begin by understanding the biomechanical factors underpinning disease. We then leverage this knowledge to pursue therapeutic candidates that target the proteins that modulate a given condition to correct the underlying defect. Our aim is to match the mechanism of the molecule to the mechanism of disease.

2) **Commit to disease-area leadership.** Our precision approach is reliant on identifying relatively homogenous subgroups of patients with shared genotypic or phenotypic disease characteristics. These subgroups, united by common biologic markers rather than just disease symptoms, may not have been previously well characterized. As our product candidates advance through clinical testing, we are building deep relationships with researchers, physicians, caregivers, advocates and patients to create an extended community dedicated to advancing diagnosis, treatment and disease management.

3) **Grow our pipeline guided by a cycle of learning that integrates clinical and molecular information with insights into disease biology.** We utilize plasma and imaging biomarkers to directly measure the effects of our product candidates and by focusing on homogenous segments of a patient population, we are able to generate robust signals early in relatively small and efficient clinical trials. We are then able to apply our insights from the clinic back into the pipeline – inspiring new molecular targets and follow-on indications.

Our Platform

Our precision medicine platform incorporates disease research, drug discovery and clinical expertise in a self-reinforcing cycle of learning that enables the iterative generation of new disease targets and clinical development candidates designed to establish early clinical proof-of-concept. By efficiently developing product candidates that target distinct biomechanical defects associated with cardiac muscle contraction, we use clinical feedback on patient genetics, response to therapy and disease presentation to refine our understanding of which patients are most likely to benefit from our product candidates. We believe this virtuous cycle is a competitive advantage that enables us to efficiently develop therapies with disease-modifying potential for heritable cardiomyopathies that could also be applied to other cardiovascular diseases.



Our lead program, mavacamten, serves as a case study for our platform approach. Data from our Phase 2 PIONEER-HCM study of mavacamten in obstructive HCM provided new insights into the mechanism of the molecule which then served as the basis of our Phase 2 MAVERICK-HCM study of mavacamten in non-obstructive HCM. In parallel, those clinical insights are being applied to our research-stage LUS-1 program and the development plans for MYK-224, our second clinical-stage HCM product candidate. The data generated from the Phase 2 MAVERICK HCM study provided us with valuable and proprietary insights that are enabling us to advance mavacamten in the non-obstructive HCM patient population, as well as to pursue a proof-of-concept study in a targeted population of heart failure patients whose condition shares many characteristics with HCM.

Our discovery process begins with a deep mechanistic understanding of how disease-causing mutations affect the biomechanical function of the heart. This starting point is then translated into screens that help us identify small molecule agents that have the potential to be optimized to restore normal biomechanical function. The most promising of these agents are then tested in preclinical animal models that we believe are translatable to and predictive of human systems. These models are also used to develop biomarkers of drug action and, when possible, disease modification, that integrate into our early clinical development strategies. Across this entire spectrum, we leverage novel insights generated from our position at the center of the cardiomyopathy ecosystem. By applying this cycle to multiple programs, we have generated a growing library of proprietary therapeutic molecules that target a wide range of potential cardiac disease-related mechanisms and that can be used to test new hypotheses arising from our clinical research.

Our Approach

Traditional Cardiovascular Drug Development

Cardiovascular disease remains the leading cause of death and disability both in the United States and globally. In the United States alone, heart diseases affect 92 million Americans and account for a $316 billion annual cost burden. Despite the increasing global burden of cardiovascular disease, investment in cardiovascular drug development has stagnated over the past two decades, resulting in a shortage of innovative therapies addressing the underlying causes of disease.

We believe that innovation in cardiovascular drug development has been hindered by the following traditional approaches:

- ***Existing therapies are designed to treat the symptoms and not the underlying cause of the disease***.
- ***Large, outcome-based studies are needed to demonstrate statistical significance, requiring lengthy and expensive trials***.
- ***In order to be commercially viable, therapies must address large populations without differentiating among patient subgroups.***

These challenges have resulted in a relatively low number of new molecular entities approved by the FDA for cardiovascular disease compared to other disease areas. In 2019, only one of the forty-eight new medicines approved by the FDA was for a cardiovascular disease indication. By way of contrast, ten of the new medicines receiving FDA approval in 2019 were new oncology drugs. We believe there is a significant opportunity to improve cardiovascular disease treatment through the use of precision medicine for the discovery and development of new treatments.

The MyoKardia Solution

We believe that our precision medicine platform can overcome many of the obstacles facing cardiovascular drug discovery and development that have resulted in a lack of cardiovascular therapeutic innovation:

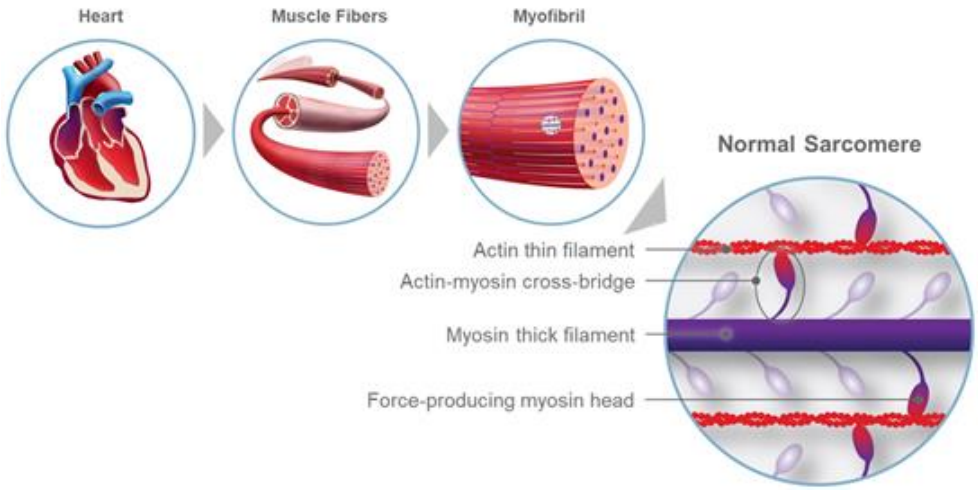
- ***Our precision medicine platform enables the discovery and development of therapies with disease-modifying potential.*** We believe our deep understanding of the biomechanical defects that cause certain cardiomyopathies and forms of heart failure allows us to target critical or causal disease mechanisms. We intend to develop each of our product candidates to prevent or reverse disease progression by correcting underlying biomechanical defects in the heart's contractile machinery.
- ***Our clinical development approach is designed to investigate efficacy and safety in smaller, less time-consuming clinical trials.*** We believe we can significantly reduce the time and cost of drug development for cardiovascular indications by targeting the underlying cause of disease, which we believe increases the chance they will be effective and reduces the potential for unintended consequences or off-target effects. Through the use of appropriate predictive biomarkers and patient selection strategies, we believe that we can reduce the risk of late-stage clinical failures. This approach is consistent with recent FDA communications and publications on how the pharmaceutical and biotechnology industry can improve efficiency and the likelihood of success in cardiovascular drug development.
- ***We are committed to disease area leadership.*** We have formed long-standing relationships with HCM patient advocacy groups and academic and clinical researchers to create an extended community dedicated to advancing our understanding of HCM. We aim to educate, foster and advance the broader HCM ecosystem, to encourage better diagnosis, better disease management and better treatment. In 2014, we launched the Sarcomeric Human Cardiomyopathy Registry (SHaRe). SHaRe is a multi-center, international repository of clinical and laboratory data on more than 9,000 individuals and family members affected by HCM and DCM, funded by research grants from MyoKardia. Data generated from SHaRe provides new insights into disease genetics, burden and progression, and is a component of our precision medicine platform.
- ***We retain global development and commercialization rights to all our programs.*** We believe consolidated control over our entire portfolio will allow us to make strategic decisions about how we advance each of our therapeutic candidates in alignment with our precision medicine approach.

Our Scientific Focus

Targeting Cardiac Muscle Contraction

Our initial research has focused on genetic mutations in sarcomeric proteins of the heart muscle. A sarcomere is an assembly of proteins that forms the smallest contractile unit of muscle. Each cardiac muscle cell contains many sarcomeres, and these cells are arranged in an organized manner as cardiac muscle fiber. Thousands of sarcomeres acting in concert provide the ensemble force for muscle contraction. Sarcomeres are composed of a thin filament and a thick filament, each of which contains multiple proteins braided together. To initiate contraction, myosin, the motor protein anchored to the thick filament, binds to actin, the main protein of the thin filament, forming a cross-bridge. The contraction of the sarcomere is driven by the swinging of the cross-bridge causing the thin filament to slide over the thick filament, shortening the length of a sarcomere. Myosin attaches to the thin filament, pulls it forward and detaches in a tightly-regulated cycle. In the heart, contraction corresponds to systole and relaxation corresponds to diastole.

In the graphic below, the dark myosin heads are engaged with the thin filament, each forming a cross-bridge between actin and myosin.



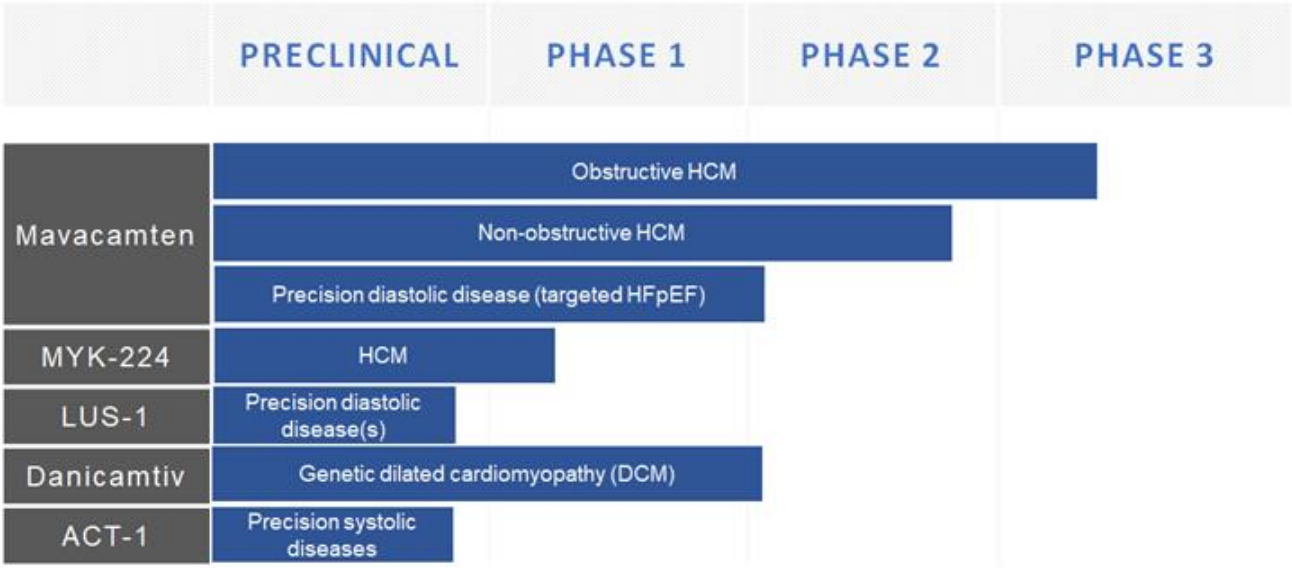
Mutations in cardiac sarcomere proteins that disrupt normal cardiac muscle contraction underpin a number of types of cardiovascular disease by affecting the power of contraction, the rate of relaxation, or both, and thereby reducing the overall ability of the heart to pump blood at an output that matches the needs of the body at rest and with exertion. The disruptions in cardiac muscle contraction result in abnormal intracardiac blood pressures and chamber volumes and thickening or thinning of the walls of the heart. These pathological changes often result in a cascade of events with devastating consequences to patients, including reduced exercise capacity limited by shortness of breath or chest pain, reduced blood flow to the heart muscle, dangerous abnormal heart rhythms, stroke, progressive heart failure and sudden cardiac death. In some patients, these events result in the need for heart transplantation.

There are hundreds of individual mutations that have been identified in the genes encoding the proteins of the sarcomere. These many mutations give rise to a few common biomechanical defects in the sarcomere at the protein level. Through our research, we have linked these biomechanical defects to three distinct cardiac muscle disruptions that act to cause the excessive contraction, impaired relaxation and/or insufficient contraction underlying many forms of heart failure.

Our Pipeline and Target Indications

We have generated several proprietary, orally administered small molecules to address a variety of biomechanical defects that cause disruptions in heart muscle contraction. By correcting the underlying biomechanical defects, we believe our targeted therapies can correct or offset the downstream disruption in cardiac muscle function that drives disease progression.

The following table summarizes our product development pipeline:



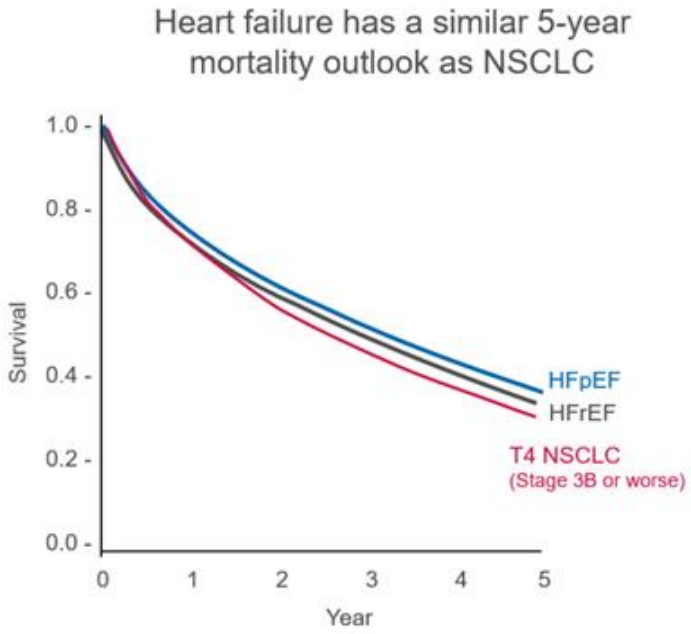
Heart Failure and Heritable Cardiomyopathies

Heart failure describes any condition in which the heart is unable to fill or pump blood sufficient to meet the needs of the body. According to the American Heart Association, heart failure affects approximately 6 million people in the United States. Even as the rate of heart disease-related mortality has slowed as the U.S. population aged 65 or over has increased, deaths associated with heart failure have increased by nearly 40% from the period 2011 to 2017. According to the Centers for Disease Control and Prevention, one in every eight deaths in the U.S. is associated with heart failure.

Systolic heart failure occurs when the left ventricle becomes distended, and the heart muscle weakens and is unable to contract with sufficient force to pump the amount of oxygenated and nutrient-filled blood the body needs. The terms systolic heart failure and dilated cardiomyopathy are sometimes used interchangeably to describe this condition. Systolic heart failure makes up a little less than half the overall heart failure population, or approximately 3 million people in the United States. Current treatment for HFrEF typically includes a regimen of multiple pills aimed at alleviating some symptoms, including the use of angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), aldosterone antagonists, beta blockers, calcium channel blockers and diuretics. More recently, angiotensin receptor-neprilysin inhibitors (ARNIs), have been introduced as another class of compounds aimed at symptom control by reducing blood pressure and helping to manage sodium and fluid levels.

Diastolic heart failure, also called heart failure with preserved ejection fraction (HFpEF), occurs when the heart is unable to properly fill with blood during the period between each contraction. The left ventricle is less distensible than normal, requiring a high pressure to fill, particularly during stress. Hypertrophic cardiomyopathy is one example of a disease in which the excess contractility of the heart has resulted in hypertrophy and stiffness that prevents the normal filling and pumping of blood. Diseases of diastolic dysfunction are estimated to affect approximately 3 million people in the United States, and there are currently no approved treatments proven to improve outcomes in patients with diastolic heart failure.

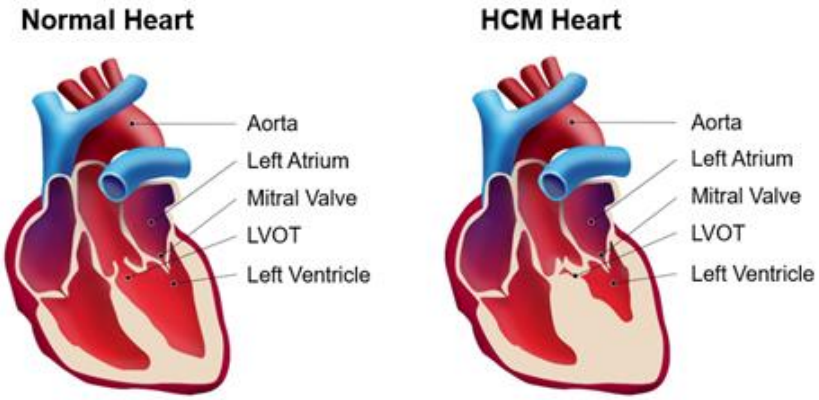
The causes of heart failure are varied and diverse and can include damage to the heart muscle from myocardial infarctions, toxic effects of cancer chemotherapy agents and genetic mutations. Symptoms associated with HFrEF and HFpEF are often similar, including shortness of breath, edema, reduction in activities and fatigue. Heart failure is progressive; once there has been an occurrence of acute decompensation, or a sudden worsening of symptoms, patients are at higher risk of further decompensation and hospitalizations, leading to death. Regardless of cause or whether it is heart failure associated with systolic or diastolic dysfunction, the five-year survival outlook for heart failure following an initial hospitalization for sudden worsening of symptoms is similar to that of Stage 4 non-small cell lung cancer as displayed below.



We believe that heart failure, whether occurring due to systolic or diastolic dysfunction, is made up of a number of distinct patient segments, each of which may be driven by shared genetic or phenotypic characteristics. Starting with heritable cardiomyopathies, such as HCM and DCM, we are discovering and developing novel targeted therapeutics tailored to address the biomechanical dysfunction in cardiac muscle contraction underlying a given condition. While some of our candidates may have broad applicability to diseases of systolic or diastolic function, our strategy is to apply a precision medicine approach to our drug development efforts. As we achieve robust signals of therapeutic activity in a given targeted population, we may seek to study adjacent populations with similar disease characteristics.

Overview of Hypertrophic Cardiomyopathy

HCM is defined as an otherwise unexplained thickening of the walls of the heart, known as hypertrophy. HCM is caused by mutations in the sarcomere that result in excessive cardiac muscle contraction. The consequences include reduced left ventricular blood volumes and cardiac output, reduced ability of the left ventricle to expand, and high cardiac filling pressures. These can all contribute to reduced effort tolerance and symptoms that include shortness of breath and chest pain. Additionally, other structural changes such as left atrial enlargement occur, leading to the development of arrhythmias and heart failure.



HCM is a chronic disease, and for the majority of patients the disease progresses slowly with the development of severe symptoms despite existing medical therapies. Mild physical exertion can quickly result in fatigue or shortness of breath, and a patient's ability to participate in normal work, family or recreational activities can be substantially curtailed. According to research published in *Circulation* by SHaRe researchers who evaluated data from nearly 4,600 patients, people with HCM have significantly higher mortality compared to that of the general U.S. population. Further, patients with genetic HCM exhibited disease at younger ages and were more likely to experience HCM-related complications and early death. In approximately 15% to 20% of patients, disease progression results in disabling heart failure that can prevent the patients from holding a job or performing everyday activities of daily living. HCM can also cause stroke or sudden cardiac death. HCM is the most common cause of sudden cardiac death in young people, with a five-year incidence among children of 3%.

HCM affects approximately one in every 500 people worldwide and is the most frequent form of heritable cardiomyopathy. It is estimated that as many as 630,000 people in the United States have a form of HCM, and based on insurance claims data, an estimated 100,000 of these individuals have been diagnosed with the disease.

Obstructive HCM Patients. In approximately two-thirds of HCM patients, the path followed by blood exiting the heart, known as the left ventricular outflow tract, or LVOT, becomes obstructed by the enlarged and diseased muscle, restricting the flow of blood from the heart to the rest of the body. Patients with this obstructive form of HCM are at increased risk for heart failure and death.

Non-Obstructive HCM Patients. Symptomatic non-obstructive, HCM patients represent a distinct subgroup that is difficult to manage medically. This segment may contain a more severely affected population because non-obstructive HCM patients are typically diagnosed when their disease is more advanced than obstructive HCM patients. Furthermore, while obstructive HCM patients often experience symptom improvement with relief of the obstruction, no such treatment option is available to non-obstructive HCM patients.

Current Standard of Care for Patients with Hypertrophic Cardiomyopathy

The current standard of care for HCM is limited, and many patients remain symptomatic. The beta-blocker propranolol is recommended for the treatment of symptomatic HCM. However, beta blockers are frequently ineffective and have off-target adverse effects that limit their use. Patients are therefore prescribed additional drugs indicated for the treatment of hypertension, heart failure or other cardiovascular disorders more generally. These drugs, including non-dihydropyridine calcium channel blockers (such as verapamil and diltiazem) and the antiarrhythmic disopyramide, do not address the underlying cause of HCM, do not appear to affect disease progression, and have limited tolerability. While clinical experience and expert opinion suggest that these drugs may provide symptom relief in some patients, no controlled clinical research evidence exists to directly support their efficacy. For a subset of HCM patients with more advanced disease progression or more pronounced symptoms, surgical or other invasive interventions may be appropriate, including heart transplantation, use of an implantable cardioverter-defibrillator, open surgical myectomy or percutaneous alcohol septal ablation.

Mavacamten for Obstructive HCM

Mavacamten is a novel, oral, allosteric inhibitor of cardiac myosin. It is intended to reduce cardiac muscle contractility by inhibiting the excessive myosin-actin cross-bridge formation that underlies the excessive contractility, left ventricular hypertrophy and reduced compliance characteristic of HCM. Mavacamten is currently being evaluated, through the pivotal Phase 3 EXPLORER-HCM study, for efficacy and safety in the treatment of symptomatic obstructive HCM. Topline data from the EXPLORER-HCM trial are anticipated in the second quarter of 2020. Pending the outcome of this study, we plan to file an NDA seeking regulatory approval of mavacamten for the treatment of obstructive HCM. Additional ongoing studies of mavacamten include the MAVA long-term extension study, the PIONEER open-label extension (OLE) study. The VALOR-HCM clinical trial, which will evaluate the potential of mavacamten to mitigate the need for invasive septal reduction procedures, is expected to begin in mid-2020.

EXPLORER-HCM is a multi-national randomized double-blind Phase 3 study designed to evaluate the efficacy and safety of 30 weeks of once-daily treatment with mavacamten in patients with obstructive HCM. Patients are randomized on a 1:1 basis to receive either mavacamten or placebo for a 30-week treatment period. The primary endpoint is a composite functional endpoint, achieved by either 1) an improvement of at least 1.5 mL/kg/min in peak oxygen consumption (peak VO_2) accompanied by an improvement from baseline of at least one NYHA functional class or 2) an improvement from baseline of 3.0 mL/kg/min or greater in peak VO_2 without worsening in NYHA functional class. Secondary endpoints include the changes from baseline in post-exercise peak LVOT gradient, NYHA functional class, and peak VO_2. Exploratory endpoints include changes in echocardiographic indices of cardiac structure and function, N-terminal pro b-type natriuretic peptide (NT-proBNP) concentrations, quality of life questionnaire scores and daily physical activity assessed using a wearable accelerometer. Following the 30-week treatment period and eight-week post-treatment wash-out period, patients will be offered the opportunity to participate in a long-term extension study of mavacamten.

The EXPLORER-HCM trial design incorporates individualized dosing, including two dose adjustments during the 30-week treatment period based on measurements of LVOT gradient. All assessments and dose adjustments are conducted in a blinded fashion. Patients are allowed to maintain their HCM-related background medications for the duration of the EXPLORER-HCM Phase 3 trial, including beta blockers or calcium channel blockers. An independent data monitoring committee has been established to monitor safety throughout the study and has met approximately every three months since EXPLORER-HCM was initiated in mid-2018. Enrollment in EXPLORER-HCM concluded in August of 2019 and enrolled a total of 251 patients with clinical sites from across 13 countries. We expect to announce topline data from the Phase 3 EXPLORER-HCM study in the second quarter of 2020.

MAVA-LTE

MAVA-LTE is a long-term extension study initiated in 2018. MAVA-LTE is enrolling patients who have completed the Phase 3 EXPLORER-HCM study or our Phase 2 MAVERICK-HCM study of mavacamten for non-obstructive HCM. The MAVA-LTE study will assess long-term safety of mavacamten, as well as its effects on symptoms and echocardiographic measures of systolic and diastolic cardiac function. We intend to enroll up to 280 patients in the MAVA-LTE study, and approximately 100 patients will be randomized to participate in a cardiac magnetic resonance imaging sub-study to assess the potential effects of mavacamten treatment on cardiac remodeling.

PIONEER-OLE

In the second quarter of 2018, we initiated an open-label study enrolling patients from our Phase 2 PIONEER-HCM clinical trial. We have presented data from the PIONEER-OLE study at twelve, twenty-four, thirty-six and forty-eight weeks. These data confirmed the results from the PIONEER-HCM study; mavacamten treatment reduced LVOT gradient to below diagnostic thresholds (30 mmHg) in the majority of patients, and below the threshold for invasive intervention (50mmHg) in all patients at all time points reported. At baseline, patients enrolled in PIONEER-OLE were symptomatic with a NYHA classification of II or III. As NYHA was evaluated at weeks 24 and 48, a majority of patients (nine of twelve) achieved Class I, or asymptomatic, status. Left ventricular ejection fraction (LVEF) remained above normal (50%) in all 12 patients at all times of assessment. Mavacamten has been well tolerated through one year of treatment. There have been no cardiac-related adverse events, and all treatment-associated adverse events have been mild-to-moderate and transient.

In addition to these observations, over the course of the PIONEER-OLE study we have noted improvements in a number of biomarkers of cardiac health moving toward normal. At Week 48:

- NT-proBNP, an established circulating blood marker of cardiac wall stress, significantly decreased to a mean of 137 pg/mL from a baseline of 594 pg/mL. A normal NT-proBNP is considered less than 125 pg/mL and NT-proBNP levels in HCM patients of <310 pg/mL have been associated with a 75% reduction in the rate of heart failure-related death or hospitalization, progression to end-stage disease, and stroke, as compared with patients with levels ≥310 pg/mL.
- E/e', an echocardiographic measure of left ventricular filling pressure, decreased with statistical significance from a mean baseline measure of 12.8 to 9.1.

- Left atrial volume index (LAVI) decreased to normal levels, from a baseline mean of 41 mL/m2 to a mean of 32 mL/m2. A normal range for LAVI is 16-34 mLm2. Left atrial volumes provide an indication of the filling pressure of the left ventricle, and increased volumes are potentially associated with an increased risk of atrial fibrillation in HCM patients.
- Reductions in interventricular septal (IVS) thickness as measured by echocardiography were observed, from a mean of 17mm at baseline to 15mm at 48 weeks of mavacamten treatment. Studies of HCM patients following septal reduction interventions have shown that IVS reductions in HCM patients are associated with improvements in LVOT gradient, functional capacity and symptoms. The risk of sudden cardiac death in HCM patients has been observed to increase progressively as wall thickness increases above 15mm.

VALOR-HCM

In September 2019, we announced our intent to study mavacamten as a therapeutic alternative to septal reduction therapy, or SRT. The VALOR-HCM study will be conducted at leading HCM centers that regularly perform surgical myectomy or alcohol septal ablation procedures, with support from the established referral networks at those centers. The randomized, double-blind study will enroll symptomatic, obstructive HCM patients referred for SRT, and MyoKardia anticipates that enrollment will begin in mid-2020. The study is being conducted in partnership with Cleveland Clinic C5 Research.

Each year, approximately 1,500 patients with obstructive HCM undergo septal reduction therapy in the United States. SRT is performed as either an open-heart surgical procedure, known as a myectomy, or injection of alcohol into the heart muscle, which causes the heart muscle cells in the thickened area to die. Both procedures are intended to reduce the thickness of the septal wall and alleviate obstruction.

PIONEER-HCM

Our Phase 2 clinical trial of mavacamten was a twelve-week open-label study to assess the efficacy, safety, pharmacokinetics, pharmacodynamics, and tolerability of mavacamten in patients with symptomatic obstructive HCM. PIONEER-HCM consisted of two dosing cohorts: in Cohort A, patients received a once-daily 10mg, 15mg or 20mg dose of mavacamten and were required to discontinue background therapy, including beta blockers, prior to study entry; in Cohort B, subjects received a once-daily 2mg or 5mg oral dose of mavacamten and nine out ten patients remained on beta blocker therapy. Baseline patient characteristics were similar across both patient cohorts.

Mavacamten achieved statistically significant changes in the primary endpoint of post-exercise LVOT gradient from baseline and demonstrated improvements across key secondary endpoints including New York Heart Association, or NYHA, functional classification, exercise capacity as measured by peak oxygen consumption, or peak VO_2, and change in dyspnea scores. The following table summarizes the data from our PIONEER-HCM Phase 2 study:

	Cohort A		**Cohort B**	
Number of patients	n=11*		n=10	
Mavacamten doses studied	10mg, 15mg, 20mg QD		2mg, 5mg QD	
Change, from baseline to W12	**Mean ± SD**	***p*-value**	**Mean ± SD**	***p*-value**
Post-exercise LVOT gradient (mmHg)	-112 ± 63.8	0.002	-25 ± 28.7	0.020
Resting LVOT gradient (mmHg)	-55 ± 41.8	0.006	-49 ± 48.0	0.004
Resting LVEF (%)	-16 ± 14.1	0.008	-5.5 ± 6.0	0.002
NYHA class	-0.9 ± 0.7	0.016	-1.0 ± 0.5	0.004
Peak VO_2 (mL/kg/min)	+3.5 ± 3.25	0.004	+1.7 ± 2.3	0.121
Dyspnea numerical rating scale	-3.1 ± 1.4	0.002	-3.0 ± 2.8	0.008
* In this first patient cohort of PIONEER-HCM, 11 patients enrolled and 10 completed the study.				

In both cohorts, mavacamten was generally well-tolerated. One patient in the Cohort A elected to stop the study drug at Week 4 after experiencing a serious adverse event that we believe was due in part to the discontinuation of background medications to control atrial fibrillation. All other adverse events, or AEs, were mild to moderate, and a majority of the AEs were deemed to be unrelated to the study drug.

Observations from the PIONEER-HCM study identified a target concentration range at which mavacamten is expected to achieve clinically meaningful improvements in obstructive HCM symptoms, functional classification (e.g., NYHA), and exercise capacity (e.g., peak VO_2) while maintaining LVEF in a normal range of greater than or equal to 50%. Data from the Phase 2 PIONEER-HCM study helped inform the starting dose, guide dose adjustment and define endpoints for our Phase 3 clinical trial of mavacamten in symptomatic obstructive HCM, known as EXPLORER-HCM. We reviewed data from our Phase 2 PIONEER-HCM clinical trial, as well as the EXPLORER-HCM study design, with the Division of Cardiovascular and Renal Products of the FDA, incorporating their input. Based on our interactions with the FDA, we believe data from the EXPLORER-HCM and MAVA-LTE studies will support our planned registrational filing with the FDA for the potential regulatory approval of mavacamten.

PHASE 1 STUDIES

Our Phase 1 program for mavacamten consisted of three clinical trials, including two single-ascending dose (SAD) trials and one multiple ascending dose (MAD) trial. Across these three trials, we dosed 86 healthy volunteers and 15 HCM patients with mavacamten, in addition to 22 subjects that received placebo. We observed favorable tolerability of single and multiple doses of mavacamten in both healthy volunteers and HCM patients and demonstrated the ability of mavacamten to reduce cardiac muscle contractility, an important biomarker of disease. Additionally, we generated preliminary evidence in two patients with obstructive HCM that led us to believe that mavacamten could reduce LVOT obstruction.

Mavacamten for Non-Obstructive HCM and Diseases of Diastolic Dysfunction

MAVERICK-HCM

Our observations from Cohort B of the PIONEER-HCM Phase 2 study, noting that even patients on low doses of mavacamten appeared to achieve improvements in symptoms and function, led to new research on mavacamten's effect on diastolic relaxation. Animal models of non-obstructive HCM provided further evidence that mavacamten is improving compliance of the left ventricle and thereby enabling the heart to better fill with oxygenated blood. In 2018 we initiated a randomized, double-blind, placebo-controlled Phase 2 clinical trial known as MAVERICK-HCM to study mavacamten in patients with symptomatic, non-obstructive HCM.

The MAVERICK-HCM study enrolled a total of 59 patients randomized into one of three cohorts, including two different target concentrations of mavacamten as well as placebo. Topline data from this study, released in November 2019, showed that mavacamten was well tolerated in this population, and the observed safety data were generally consistent with observations from prior studies. Over the course of 16 weeks of study, a statistically significant reduction in NT-proBNP was observed versus placebo. In two subgroups of patients with more severe diastolic impairment – one with elevated cardiac filling pressures and a pre-specified group of patients at higher risk for morbidity and mortality -- improvements in diastolic function and clear signals of clinical benefit were observed.

Based on the safety and pharmacologic benefits observed in MAVERICK-HCM, and a growing body of preclinical and clinical data indicating that mavacamten may provide benefit to individuals with diastolic dysfunction, we plan to advance mavacamten into additional studies in defined groups of patients with non-obstructive HCM and HFpEF. We plan to initiate a Phase 2 study in the second quarter of 2020 in a subgroup of patients with HFpEF who share many characteristics with the subgroups identified in MAVERICK-HCM. We plan to review the data from MAVERICK-HCM with the FDA and to discuss plans for the late-stage clinical evaluation of mavacamten in patients with non-obstructive HCM. Subject to the outcome of our discussions with the FDA, we anticipate beginning a pivotal program for non-obstructive HCM in the second half of 2020.

MYK-224 for HCM

MYK-224 is our second small molecule program targeting hypercontractility and impaired relaxation. In August 2019, we commenced dosing healthy volunteers in a Phase 1 study of MYK-224 for the treatment of HCM. The randomized, placebo-controlled Phase 1 study is designed to compare the safety, tolerability, and pharmacokinetics of MYK-224. MYK-224 is designed with distinct physicochemical properties that may enable certain dosing advantages for some HCM patients. In preclinical studies, MYK-224 was shown to attenuate hyperactive myosin proteins containing known pathogenic HCM mutations. MYK-224 also modulates cardiac myosin without affecting myosin-actin cross-bridge kinetics or altering calcium homeostasis. We anticipate providing topline results from the Phase 1 study in the third quarter of 2020 and believe MYK-224 may be suited for future development in HCM or HFpEF populations.

LUS-1 for HCM

LUS-1 is our preclinical program to counteract a muscle abnormality that results in impaired relaxation of the left ventricle. Our LUS-1 discovery-stage program is identifying novel therapeutics that target diastolic relaxation without reducing the force of contraction. In preclinical studies of LUS-1 molecules, we have observed improved compliance without a loss of stroke volume. LUS-1 is intended to counteract a muscle disruption that results in impaired relaxation of the heart, a biomechanical defect thought to be a causal factor in numerous types of diastolic heart failure, as well as specific HCM patient subgroups and less common heritable cardiomyopathies.

Overview of Dilated Cardiomyopathy

The fundamental cause of all systolic heart failure is that the heart muscles are not able to contract with sufficient force. In DCM, the loss of contractility leads the walls of the left ventricle to become thin and over-expanded, functioning under increased stress. This leads to even further progression of cardiac dysfunction. In contrast to HCM, some forms of DCM are characterized by decreased power output of the sarcomeres. In some patients with genetic DCM, this lack of power is caused by genetic mutations that disrupt the ability of individual myosin motors to form cross-bridges with actin and contribute to overall contraction. Genetic abnormalities contributing to DCM are estimated to be present in about 30 to 40% of DCM patients, corresponding to an estimated prevalence of 250,000 to 500,000 people in the United States. Further, genetic mutations of the sarcomere impair the ability of the heart muscle proteins to function effectively, leading to progressive worsening of function.

Dilated cardiomyopathy is a life-threatening progressive disease. Once symptoms appear, a patient's condition typically declines steadily over the next few years. Typical symptoms include shortness of breath, fatigue, swelling in the extremities or an irregular heartbeat. As the disease progresses, patients become increasingly debilitated and experience persistent shortness of breath, even at rest. Diastolic function, or the heart's ability to relax and fill with blood, is also impaired because the left ventricle is already distended. The dilated left ventricle is itself deprived of an adequate supply of oxygen that may contribute to fibrosis and the risk of dangerous heart rhythm disturbances. In addition, regardless of whether symptoms have appeared, patients with dilated cardiomyopathy are at risk of sudden cardiac death.

Current Standard of Care for Patients with Dilated Cardiomyopathy

There are no approved therapies that target the underlying cause of DCM. Dilated cardiomyopathy patients are typically prescribed one or more drugs indicated for the treatment of systolic heart failure generally, such as diuretics, beta blockers, angiotensin receptor-neprilysin inhibitors, angiotensin converting enzyme inhibitors and aldosterone antagonists. By treating various signs and symptoms of heart disease, these drugs may reduce overall morbidity and mortality; however, none of the treatments address the underlying cause of disease or eliminate disease progression. While pharmacologic therapies developed over the past 35 years have improved both the prognosis and quality of life of DCM patients, five-year mortality rates still approach 50% in community-based studies. Surgical or interventional options available to DCM patients include use of an implantable cardioverter-defibrillator, a biventricular pacemaker, and in refractory patients, a left ventricular assist device and cardiac transplant. Dilated cardiomyopathy, regardless of cause, is the most common diagnosis in patients requiring either mechanical circulatory support or a cardiac transplant.

Our portfolio of precision cardiovascular therapeutics includes multiple cardiac muscle activator programs aimed at increasing contraction of the heart muscle and thereby improving blood flow from the heart. We are initially targeting precision indications in systolic heart failure and specifically, dilated cardiomyopathies.

Danicamtiv for DCM

Danicamtiv is our lead activator candidate designed to increase the contractility of the heart (systolic function) with minimal or no effect on myocardial relaxation and compliance (diastolic function) by acting directly on the proteins in the heart muscle responsible for contraction. Danicamtiv is currently advancing into a Phase 2 clinical study in patients with certain genetic mutations of the cardiac sarcomere.

An interim analysis of 26 patients with stable heart failure due to left ventricular systolic dysfunction in the Phase 2a clinical trial showed that danicamtiv demonstrated improvement in systolic function without impacting diastolic function. These results are consistent with data from our Phase 1 single-ascending dose studies of danicamtiv in both healthy volunteers and DCM patients. Given the favorable safety profile observed to date, the Phase 2a study has been extended to evaluate higher exposures of danicamtiv. We anticipate presenting data from the Phase 2a clinical trial in the second quarter of 2020.

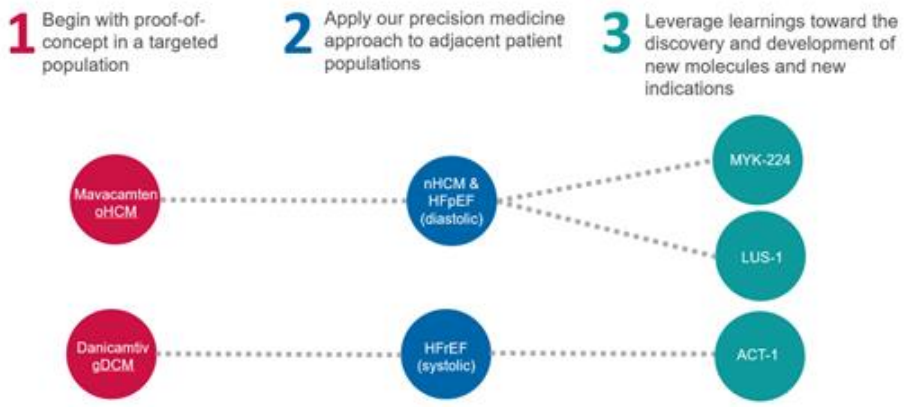
Danicamtiv is an oral, small molecule, allosteric activator of myosin. In the heart, myosin is the motor protein that binds to actin to generate the force and movement of contraction. Danicamtiv has been shown to activate myosin-actin cross-bridge formation, thereby targeting the biomechanical defects underlying disease with the intent of improving cardiac contractility. This activity has been observed in the setting of multiple pathogenic DCM mutations, as well as in a genetically normal background. In preclinical studies and early-stage clinical studies, danicamtiv improved myocardial contractility without impairing the heart's ability to relax and fill. We believe this profile, increasing the heart's contractility with minimal impact on relaxation, is distinct and differentiated from other activator or positive inotropic agents.

ACT-1 for Genetic DCM

ACT-1 is our preclinical activator program targeting DCM due to sarcomeric mutations and impaired calcium regulation. In preclinical models, our ACT-1 prototype molecules successfully increase contractility without prolonging systolic ejection time and with minimal impact on relaxation. ACT-1 is a non-myosin cardiac muscle activator intended to target a specific mutation underlying genetic forms of DCM. In preclinical studies, ACT-1 was able to increase stroke volume and systolic function with no prolongation of systolic ejection time and no significant impact on diastolic relaxation. ACT-1 has been designed specifically for genetic DCM patient segments, which will be supported based on longitudinal studies in genetic animal models. We plan to advance ACT-1 into clinical development in 2021.

Additional Potential Extensions of our Platform

We believe that the fundamental mechanisms we are targeting in the heart may have applicability in the broader heart failure population. As we accumulate data from our clinical studies and expand our knowledge of how our product candidates' mechanisms are working within the heart, we are able to look at patient populations with similar disease characteristics and consider expanding our initial target indication. We are successfully deploying this approach in the development of mavacamten – leveraging observations from our Phase 2 clinical trial in obstructive HCM to evaluate mavacamten in non-obstructive HCM patients and now moving into a subset of patients with HFpEF where the underlying cause of patient symptoms is similar to that of non-obstructive HCM.



Commercial Rights to Our Portfolio

We have discovered all of the compounds in our pipeline internally and retain global development and commercialization rights to all of our programs. We believe consolidated control over our entire portfolio will allow us to make strategic decisions about how we advance each of our therapeutic candidates in alignment with our precision medicine approach. We may enter into strategic alliances in the future for certain programs where the potential therapeutic indications do not align with our precision medicines strategy or for specific therapeutic indications or geographic territories.

Intellectual Property

For the pharmaceutical products we develop and commercialize as a normal course of business, we intend to pursue composition-of-matter patents, where possible, and dosage and formulation patents, as well as manufacturing patents and method-of-use patents on novel indications for known compounds. We also seek patent protection with respect to novel biological discoveries, including new diagnostic methods and targets. We may also pursue patents with respect to our proprietary screening and drug development processes and technology. We may also seek patent protection, either alone or jointly with our collaborators, as our collaboration agreements may dictate.

Our patent portfolio includes five issued U.S. patents, five U.S. pending patent applications, two pending Patent Cooperation Treaty (PCT) applications, over 65 foreign patent applications and patents, all of which are exclusively owned by us, and some of which have claims relating to all of our current clinical-stage drug candidates. With respect to our lead drug candidates in the HCM program, we exclusively own two issued U.S. patents, have three pending U.S. patent applications, and own over 35 foreign patent applications and patents relating to the chemical composition of mavacamten and danicamtiv and use thereof.

Individual patents extend for varying periods depending on the date of filing of the patent application and the legal term of patents in the countries in which they are obtained. Generally, patents issued for applications filed in the United States are effective for twenty years from the earliest effective filing date of the utility patent application. In addition, in certain instances, a patent term can be extended to recapture a portion of the term effectively lost as a result of the FDA regulatory review period. However, the restoration period cannot be longer than five years and the total patent term including the restoration period must not exceed 14 years following FDA approval. The duration of foreign patents varies in accordance with provisions of applicable local law, but typically is also twenty years from the earliest effective filing date of the utility patent application. Our currently issued U.S. patents with respect to mavacamten are expected to expire in 2034, not including any extensions due to patent restoration or regulatory exclusivities. However, the actual protection afforded by a patent varies on a product by product basis, from country to country, and depends upon many factors, including, but not limited to, the type of patent, the scope of its coverage, the availability of regulatory related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent.

Manufacturing

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We use third-party contract manufacturing organizations (CMOs) for all of our requirements of raw materials, drug substance and drug product for our preclinical research and our ongoing clinical trials of mavacamten, danicamtiv and MYK-224, and in 2020 will depend solely upon our CMOs due to the termination of our collaboration agreement with Sanofi. We have not entered into long-term agreements with our current CMOs. We intend to continue to rely on CMOs and may seek to enter into arrangements with strategic partners for later-stage development and commercialization of mavacamten and danicamtiv, as well as the development and commercialization of any other product candidates that we may identify. Although we currently rely on CMOs, we have personnel and third-party consultants with extensive manufacturing experience to oversee the manufacturing relationships and activities.

We believe the synthesis of the drug substance for mavacamten is reliable and reproducible. It employs readily available starting materials, and the synthetic routes are amenable to large-scale production and do not require unusual equipment or handling in the manufacturing process. We continue to obtain an adequate supply of the drug substance for mavacamten from our CMO to satisfy additional anticipated clinical demands. The current drug substance manufacturing process is the one we intend to use for commercial production. Process performance qualification and validation campaigns have been initiated. In addition, we believe the synthesis of the drug substance for danicamtiv is reliable and reproducible. We have obtained an adequate supply of the drug substance for danicamtiv from Sanofi, our former collaboration partner, to satisfy our immediate clinical and preclinical demands and have transferred the process to a CMO to produce additional supplies. We are developing improvements to our danicamtiv drug substance manufacturing process to enhance production capacity so that it will be adequate to meet future development and commercial demands. We believe the process for production of MYK-224 drug substance is also sound and scalable. The current CMO has enough supply on hand to meet the needs of Phase 1 clinical development as well as ongoing pre-clinical studies.

Drug product formulation development for mavacamten is complete and development for danicamtiv and MYK-224 is in progress. We have contracted with a third-party manufacturer capable of both formulation development and drug product manufacturing through early commercialization for mavacamten. We may identify other drug product manufacturers in the future to add additional capacity and redundancy to our supply chain. In our SAD clinical trials of mavacamten, we utilized a suspension formulation. We developed and manufactured multiple strengths of an immediate release tablet for use in the MAD and other early stage trials (including PIONEER-HCM) trial. For the EXPLORER-HCM Phase 3 study and commercialization, we have developed a refined capsule formulation and may develop alternate formulations for the adolescent and children/infant populations. We also employed a suspension formulation for the healthy volunteers SAD study of danicamtiv. We also developed an immediate release tablet formulation which is being used for the Phase 2 proof-of-concept studies in patients. We have successfully transferred danicamtiv tablet production from Sanofi to a CMO. For future danicamtiv development and commercialization, we intend to develop a refined tablet formulation and may develop alternate formulations for the adolescent and children and infant populations. As with the earlier programs, a suspension formulation is being used for the MYK-224 first in human studies. Solid oral dosage form development is underway for Phase 2 clinical studies.

Sales and Marketing

We believe that we can maximize the value of our products by retaining substantial commercialization rights to our product candidates and, where appropriate, entering into collaborations for specific therapeutic indications or geographic territories.

Our current strategy is to market our initial HCM and DCM products using a dedicated, direct sales force focused on cardiomyopathy specialists and targeted cardiologists treating HCM and DCM. These physicians include those affiliated with academic institutions, leading hospitals and medical centers as well as community cardiologists treating a significant volume of HCM and DCM patients. We believe they represent a concentrated prescriber base that can be appropriately managed with a specialty care sales model.

We are initially pursuing market approval and commercialization in the U.S. We have also begun hiring a team based in Europe to evaluate the regulatory and market opportunity, in order to inform our commercialization plans in the European Union.

Competition

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our scientific knowledge, technology and development experience, our precision medicine platform and our pioneering culture provide us with competitive advantages, we face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions, governmental agencies and public and private research institutions. Any therapeutic candidates that we successfully develop and commercialize will compete with existing products and new products that may become available in the future.

In the field of heart failure drug development, our principal competitors include Amgen Inc., AstraZeneca plc, Bayer AG, Bristol-Myers Squibb Company, C.H. Boehringer Sohn AG & Co. KG, Eli Lilly and Company, Novartis AG and Takeda Pharmaceutical Company Limited. Specific to our initial drug discovery and development focus areas, we believe that Cytokinetics, Inc., Takeda Pharmaceutical Company Limited and Novartis AG have ongoing programs in HCM and that Novartis AG, Pfizer Inc., Tenaya Therapeutics, Berlin Cures, and Zensun (Shanghai) Sci. & Tech. Co., Ltd. have ongoing programs in DCM. Additionally, there may be other companies pursuing therapeutic candidates from which we face current or future competition.

Government Regulation

Government authorities in the United States at the federal, state and local levels, and in other countries, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, marketing, export and import of drug products such as those we are developing.

A number of different regulatory agencies may have regulatory oversight, depending on the product at issue, and the type and stage of activity. In the United States, these include the FDA, the Drug Enforcement Administration (DEA), the Centers for Medicare and Medicaid Services (CMS), other federal agencies, state boards of pharmacy, state-controlled substance agencies and more.

Drug Development Regulation

Drug Development Process

The pharmaceutical industry is subject to extensive global regulation by regional, country, state and local agencies. In the United States, the FDA is the primary regulator of drugs under the Federal Food, Drug, and Cosmetic Act, or the FDCA, and implementing regulations. The process of obtaining regulatory approvals and compliance with applicable federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources.

The process required before a drug may be marketed in the United States, the EU and most foreign countries generally involves the following:

- completion of preclinical, also known as nonclinical, laboratory tests, animal studies and formulation studies conducted according to Good Laboratory Practice (GLP) requirements, animal welfare laws and other applicable regulations;
- submission to the FDA of an IND, which must become effective before clinical trials, meaning trials in human subjects, may begin in the United States, obtaining similar authorizations in other jurisdictions where clinical research will be conducted and maintaining these authorizations on a continuing basis throughout the time that trials are performed, and new data are collected;
- performance of adequate and well-controlled clinical trials according to Good Clinical Practice (GCP) requirements to demonstrate whether a proposed drug is safe and effective for its intended use;
- preparation and submission to the FDA of an NDA, and submitting similar marketing authorization applications in other jurisdictions where commercialization will be pursued;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product will be produced to assess compliance with current good manufacturing practice (cGMP) and/or similar requirements in other jurisdictions where commercialization will be pursued, to assure that the facilities, methods and controls are adequate to preserve the product’s identity, strength, quality and purity;

- satisfactory completion of an FDA or other regulatory authority inspection of clinical trial sites to assess compliance with GCP requirements; and
- FDA review and approval of the NDA or other regulatory authority review and approval of a marketing authorization application.

The development, testing and approval process requires substantial time, effort and financial resources and bears significant and inherent risk that the individual products will not exhibit the relevant safety, effectiveness, or quality characteristics. The approval process may be more or less rigorous from country to country, and the time required for approval may be longer or shorter than that required in the United States. Approval in one country does not assure that a product will be approved in another country. We cannot be certain that any approvals for our product candidates will be granted on a timely basis, or with the specific terms that we desire, if at all.

An IND is a request for authorization from the FDA to administer an investigational drug product to humans. FDA's primary objectives in reviewing an IND are, in all phases of the investigation, to assure the safety and rights of subjects, and, in Phase 2 and 3, to help assure that the quality of the scientific evaluation of drugs is adequate to permit an evaluation of the drug's effectiveness and safety. The central focus of an IND submission is on the general investigational plan and the protocol(s) for clinical trials. The IND also includes results of animal studies or other human studies, as appropriate, as well as manufacturing information, analytical data and any available clinical data or literature to support the use of the investigational new drug. An IND must become effective before human clinical trials may begin. An IND will automatically become effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to the proposed clinical trials. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before clinical trials can begin. The FDA also may impose a clinical hold after a trial has started. Accordingly, submission of an IND may or may not result in the FDA allowing clinical trials to commence.

Clinical trials involve the administration of the investigational drug to human subjects under the supervision of qualified investigators in accordance with GCP, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the inclusion and exclusion criteria, the parameters to be used in monitoring safety, and the efficacy criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND, or to the governing authorities on a country by country basis. Additionally, approval must also be obtained from each clinical trial site’s institutional review board (IRB) or ethics committee (EC) before the trials may be initiated, and the IRB or EC must monitor the study until completed.

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

- Phase 1. The drug initially is introduced into a small number of patients or healthy human volunteers. These trials are designed to determine the metabolism and pharmacologic actions, side effects with increasing doses and if possible, early evidence of effectiveness.
- Phase 2. These trials include controlled clinical trials initiated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the effectiveness of the drug candidate for a particular indication in patients with the disease or condition under study, and to determine common short-term side effects and risks associated with the drug.
- Phase 3. Clinical trials are expanded, and controlled trials undertaken to further evaluate dosage, clinical efficacy and safety. These clinical trials are intended to gather additional information about effectiveness and safety that is needed to evaluate the overall benefit-risk profile of the drug candidate and provide an adequate basis for physician labeling and regulatory approval.
- Regulatory agencies may also require, or companies may pursue, additional clinical trials after a product is approved.

During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data, and clinical study investigators. Progress reports related to clinical trials must be submitted at least annually to the FDA and participating IRBs, and other governing authorities. IND safety reports must be submitted to the FDA and other governing health authorities and to investigators for serious and unexpected suspected adverse events, findings from animal or in vitro testing or other studies that suggest a significant risk to humans exposed to the drug, and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report to the FDA within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor’s initial receipt of the information. The FDA or other governing authorities or the sponsor may suspend a clinical trial at any time for a variety of reasons, including a finding that human subjects are being exposed to an unacceptable health risk or that the

investigational product apparently lacks efficacy. Similarly, an IRB or EC can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with applicable requirements or if the drug candidate has been associated with unexpected serious harm to healthy volunteers or patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data monitoring committee (DMC). The DMC reviews safety information and provides recommendations to the sponsor for whether a trial may move forward at designated check points based on access to certain data from the study.

A manufacturer of an investigational drug for a serious disease or condition is required to make available, such as by posting on its website, its policy on evaluating and responding to requests for individual patient access to such investigational drug. This requirement applies on the earlier of the first initiation of a Phase 2 or Phase 3 trial of the investigational drug or, as applicable, 15 days after the drug receives a designation as a breakthrough therapy, fast track product, or regenerative advanced therapy.

At times during the development of a new drug product, sponsors are given opportunities to meet with the FDA. This commonly occurs prior to submission of an IND, at the end of Phase 2 trials, and before an NDA is submitted. Meetings at other times may also be requested. These meetings provide an opportunity for the sponsor to share information about the data gathered to date and for the FDA to provide advice, including feedback on the next phase of development. Concurrent with clinical trials, companies usually complete additional animal studies and develop additional information about the chemistry and physical characteristics of the drug candidate and finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate. Additionally, appropriate packaging must be selected and tested, and stability trials must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf-life and distribution pathway. There are also requirements governing the reporting of certain clinical trials and completed clinical trial results to public registries, such as clinicaltrials.gov.

The results of drug candidate development, preclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the drug candidate, proposed labeling and other relevant information are submitted to the FDA as part of an NDA, requesting approval to market the drug candidate for one or more proposed indications. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and effectiveness of the investigational drug product to the satisfaction of the FDA.

Under the Prescription Drug User Fee Act (PDUFA) as amended, each NDA must be accompanied by a user fee (adjusted by the FDA on an annual basis). According to the FDA's fee schedule, effective through September 30, 2020, the user fee for each NDA application requiring clinical data is $2,942,965. For fiscal year 2020, PDUFA also imposes an annual prescription drug product program fee of $325,424. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on NDAs for products designated as orphan drugs, unless the product also includes a non-orphan indication.

The FDA reviews each NDA to ensure that it is sufficiently complete for substantive review before it may be filed. Once the submission is accepted for filing, the FDA begins an in-depth review. The FDA's goal is to review applications within ten months of the filing date or, if the application relates to an unmet medical need in a serious or life-threatening indication and is granted priority review, six months from the filing date. The review process is often significantly extended by FDA requests for additional information or clarification. The FDA reviews an NDA to determine, among other things, whether a drug candidate is safe and effective for its intended use and indication for use and whether its manufacturing is cGMP-compliant. The FDA may refer the NDA to an advisory committee consisting of a panel of external experts for review and recommendation as to whether the NDA should be approved and under what conditions. The FDA is not bound by the recommendation of an advisory committee, but it typically follows such recommendations.

After the FDA evaluates the NDA and conducts inspections of manufacturing facilities where the drug product and/or its active pharmaceutical ingredient will be produced, it may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete, and the application is not ready for approval. A Complete Response Letter identifies deficiencies that may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical trial(s), and/or other significant, expensive and time-consuming requirements related to clinical trials, preclinical studies or manufacturing. Even if such additional 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.

Expedited Development and Review Programs

The FDA has various programs, including fast track, priority review, accelerated approval, and breakthrough therapy designation, that are intended to facilitate and expedite development and review of new drugs to address unmet medical need in the treatment of a serious or life-threatening condition. Even if a drug candidate qualifies for one or more of these programs, the FDA may later decide that the drug candidate no longer meets the conditions for qualification. Fast Track designation, priority review, accelerated approval and breakthrough therapy designation do not change the standards for approval but may expedite the development or approval process.

The Fast Track program is intended to expedite or facilitate the process for reviewing new drugs that are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast Track designation applies to the combination of the product and the specific indication for which it is being studied. The sponsor of a new drug may request the FDA to designate the drug as a Fast Track product at any time during the clinical development of the product. Unique to a Fast Track product, the FDA may consider for review sections of the marketing application on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the application, the FDA agrees to accept sections of the application and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the application.

Any product for a serious or life-threatening condition 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 designated for priority review in an effort to facilitate the review.

Drug candidates 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 studies 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 that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require that a sponsor of a drug receiving accelerated approval perform adequate and well-controlled post-marketing clinical studies. Failure to conduct required post-approval trials, or the inability to confirm a clinical benefit during post-marketing trials, may allow the FDA to withdraw the drug from the market on an expedited basis. In addition, the FDA presently requires as a condition for accelerated approval pre-approval of promotional materials.

A drug can be designated as a breakthrough therapy if it is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that it may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. A sponsor may request that a drug be designated as a breakthrough therapy at any time during the clinical development of the product. If so designated, FDA shall act to expedite the development and review of the product's marketing application, including by meeting with the sponsor throughout the product's development, providing timely advice to the sponsor to ensure that the development program to gather preclinical and clinical data is as efficient as practicable, involving senior managers and experienced review staff in a cross-disciplinary review, and assigning a cross-disciplinary project lead for the FDA review team to facilitate an efficient review of the development program and to serve as a scientific liaison between the review team and the sponsor.

Post-Approval Requirements

Any products for which we may receive future FDA approval are subject to continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting and analysis of adverse experiences with the product, providing the FDA with updated safety, efficacy and quality information, product sampling and distribution requirements, maintaining up-to-date labels, warnings, and contraindications, and complying with promotion and advertising requirements. Products may be promoted only for the approved indications and in accordance with the approved label; products cannot be promoted for unapproved, or off-label, uses, although physicians may prescribe drugs for off-label uses in accordance with the practice of medicine. Manufacturers must continue to comply with cGMP requirements, which are extensive and require considerable time, resources and ongoing investment to ensure compliance. In addition, changes to manufacturing processes often 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. In addition, the FDA may require testing and surveillance programs to monitor the effect of approved products that have been commercialized, and the FDA has the power to prevent or limit further marketing of a product based on the results of these post-marketing programs. Manufacturers and other entities involved in the manufacturing and distribution of approved products are required to register their establishments with the FDA and certain state agencies and are subject to periodic inspections for compliance with cGMP and other laws. FDA and state inspections may identify compliance issues at manufacturing facilities that may disrupt production or distribution or may require substantial resources to correct.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements is not maintained or if problems occur after the product reaches the market, such as adverse events, the existence or severity of which was unknown when the product was approved. Later discovery of previously unknown problems with a product may result in restrictions on the product, revised labeling or complete withdrawal from the market. Further, the failure to maintain compliance with regulatory requirements may result in administrative or judicial actions, such as fines, warning letters, clinical trial holds, voluntary product recalls, product seizures, product detention or refusal to permit the import or export of products, refusal to approve pending applications or supplements, restrictions on marketing or manufacturing, injunctions or civil or criminal payments or penalties.

From time to time, new legislation is enacted that changes the statutory provisions governing the approval, manufacturing, and marketing of products regulated by the FDA. In addition, FDA regulations and guidance may be revised or reinterpreted by the agency in ways that may significantly affect our business and our products. It is impossible to predict whether further legislative or regulatory or policy changes will occur or be implemented and what the impact of such changes, if any, may be.

Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration, and specifics of 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, referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent term to be extended up to five years as compensation for patent term effectively lost due to the FDA's pre-market approval requirements. 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, except that the review period is reduced by any time during which the applicant failed to exercise due diligence. Only one patent applicable to an approved drug is eligible for the extension. Extensions are not granted as a matter of right and the extension must be applied for prior to expiration of the patent and within a 60-day period from the date the product is first approved for commercial marketing. The United States Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. Where a product contains multiple active ingredients, if any one active ingredient has not been previously approved, it can form the basis of an extension of patent term provided the patent claims that ingredient or the combination.

Market exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The specific scope varies, but fundamentally the FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity never previously approved by the FDA either alone or in combination. 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 compound 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. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA, or supplement to an existing NDA if new clinical investigations, other than bioavailability trials, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, for 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 Information and Exclusivity

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 and may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA-issued "Written Request" for such a trial. The FDA issues a written request for pediatric clinical trials prior to approval of an NDA only where it determines that information relating to the use of a drug in a pediatric population, or part of the pediatric population, may produce health benefits in that population.

Under the FDCA, NDAs and certain supplements to NDAs must contain data adequate 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 drug is safe and effective. The FDCA requires that a sponsor who is planning to submit a marketing application for a drug or biological product that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration submit an initial Pediatric Study Plan (PSP), unless the drug has been granted orphan designation for the proposed indication at the time the initial PSP is required, within 60 days of an end-of-Phase 2 meeting or as may

be agreed between the sponsor and the FDA. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. The FDA and the sponsor must reach agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from preclinical studies, early phase clinical trials, and/or other clinical development programs.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drug candidates 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 costs of research and development of the drug for the indication can be recovered by sales of the drug in the United States. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a drug candidate that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication for seven years, except in very limited circumstances, such as if the second applicant demonstrates the clinical superiority of its product or the manufacturer of the product with exclusivity is unable to assure sufficient quantities of the product. Orphan drug exclusivity does not prevent the FDA from approving a different drug for the same disease or condition, or the same drug for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the NDA application user fee. Orphan drug exclusivity could block the approval of our drug candidates for seven years if a competitor obtains approval of the same product as defined by the FDA or if our drug candidate is determined to be contained within the competitor’s product for the same indication or disease.

As in the United States, we may apply for designation of a drug candidate as an orphan drug for the treatment of a specific indication in the European Union before the application for marketing authorization is made. In the EU, the European Commission, after reviewing the opinion of the EMA’s Committee for Orphan Medicinal Products, granted orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions affecting not more than 5 in 10,000 persons in the EU Community (or where it is unlikely that the development of the medicine would generate sufficient return to justify the investment) and for which no satisfactory method of diagnosis, prevention, or treatment has been authorized (or, if a method exists, the product would be a significant benefit to those affected). Orphan drug designation in the EU entitles the manufacturer to financial incentives such as reduction of fees or fee waivers and up to 10 years of market exclusivity for the approved indication unless another applicant can show that its product is safer, more effective or otherwise clinically superior to the orphan designated product. This period may be reduced to six years if the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. Orphan drug designation must be requested before submitting an application for marketing approval. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The FDA and foreign regulators expect holders of exclusivity for orphan drugs to assure the availability of sufficient quantities of their orphan drugs to meet the needs of patients. Failure to do so could result in the withdrawal of marketing exclusivity for the orphan drug.

Pharmaceutical Coverage, Pricing, and Reimbursement

United States

Significant uncertainty exists as to the coverage and reimbursement status of any products for which we obtain regulatory approval. In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use our products unless coverage is provided, and reimbursement is adequate to cover a significant portion of the cost of our products. Sales of any products for which we receive regulatory approval for commercial sale will therefore depend, in part, on the availability of coverage and adequate reimbursement from third-party payors such as government health programs, commercial or private insurance, and managed care organizations. Third-party payors include government authorities, managed care providers, private health insurers and other organizations.

In the United States, no uniform policy of coverage and reimbursement for drug products exists, and one payor's determination to provide coverage and adequate reimbursement for a product does not assure that other payors will make a similar determination. Accordingly, decisions regarding the extent of coverage and amount of reimbursement to be provided for any of our products will be made on a payor-by-payor basis. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the FDA-approved drugs for a particular indication. A decision by a third-party payor not to cover our product candidates could reduce physician utilization of our products once approved and have a material adverse effect on our sales, results of operations and financial condition. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development. Many private payors, however, use coverage decisions and payment amounts determined by the CMS as guidelines in setting their coverage and reimbursement policies. The coverage determination process will require us to provide scientific and clinical support for the use of our products to each payor separately and will be a time-consuming process.

The marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, we expect that an increasing emphasis on cost containment measures in the United States will continue to increase the pressure on pharmaceutical pricing. Third-party payors are increasingly challenging the prices charged for products and services, examining the medical necessity and reviewing the cost-effectiveness of drugs, medical devices and medical services, in addition to questioning safety and efficacy. If these third-party payors do not consider our products to be cost-effective compared to other available therapies, they may not cover our products after FDA approval or, if they do, the level of payment may not be sufficient to allow us to sell our products at a profit. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

European Union

In Europe and many other foreign countries, the success of our drug candidates we may develop depends largely on obtaining and maintaining government reimbursement, because in many foreign countries patients are unlikely to use prescription pharmaceutical products that are not reimbursed by their governments. Negotiating reimbursement rates in foreign countries can delay the commercialization of a pharmaceutical product and generally results in a reimbursement rate that is lower than the net price that companies can obtain for the same product in the United States.

In some countries, such as Germany, commercial sales of a product can begin while the reimbursement rate that a company will receive in future periods is under discussion. In other countries, a company must complete the reimbursement discussions prior to the commencement of commercial sales of the pharmaceutical product. 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 drugs for which their national health insurance systems provide reimbursement and to control the prices of drugs for human use. A member state may approve a specific price for the drug or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the drug on the market. Recently, many countries in the European Union have increased the number of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the European Union. 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, if approved in those countries.

Other Federal and State Healthcare Laws, Including Anti-Kickback, Fraud and Abuse and Health Information Privacy and Security Laws

In addition to FDA restrictions on marketing of pharmaceutical products, pharmaceutical companies also are subject to various federal and state laws pertaining to healthcare fraud and abuse, including anti-kickback laws and false claims laws, and the reporting of payments to physicians and teaching hospitals. In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business. If our operations are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to penalties, including, without limitation, administrative, civil and criminal penalties, damages, fines, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, the curtailment or restructuring of our operations, exclusion from participation in federal and state healthcare programs and individual imprisonment, any of which could adversely affect our ability to operate our business and our financial results.

In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, collectively, ACA, was enacted, which includes measures that have significantly changed the way health care is financed by both governmental and private insurers. Among the provisions of ACA of greatest importance to the pharmaceutical industry are the following:

The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of the Department of Health and Human Services, a condition for states to receive federal matching funds for the manufacturer's outpatient drugs furnished to Medicaid patients. Effective in 2010, ACA made several changes to the Medicaid Drug Rebate Program, including increasing pharmaceutical manufacturers' rebate liability by raising the minimum basic Medicaid rebate on most branded prescription drugs and biologic products from 15.1% of average manufacturer price (AMP) to 23.1% of AMP and adding a new rebate calculation for "line extensions" (i.e., new formulations, such as extended release formulations) of solid oral dosage forms of branded products, as well as potentially impacting their rebate liability by modifying the statutory definition of AMP. ACA also expanded the universe of Medicaid utilization subject to drug rebates by requiring pharmaceutical manufacturers to pay rebates on Medicaid managed care utilization as of 2010 and by expanding the population potentially eligible for Medicaid drug benefits. In addition, the ACA provides for the public availability of retail survey prices and certain weighted average AMPs under the Medicaid program. The implementation of this requirement by the CMS may also provide for the public availability of pharmacy acquisition of cost data, which could negatively impact our sales.

In order for a pharmaceutical product to receive federal reimbursement under the Medicare Part B and Medicaid programs or to be sold directly to United States government agencies, the manufacturer must extend discounts to entities eligible to participate in the 340B drug pricing program. The required 340B discount on a given product is calculated based on the AMP and Medicaid rebate amounts reported by the manufacturer. Effective in 2010, ACA expanded the types of entities eligible to receive discounted 340B pricing, although, under the present state of the law, with the exception of children's hospitals, these newly eligible entities will not be eligible to receive discounted 340B pricing on orphan drugs when used for the orphan indication. In addition, as 340B drug pricing is determined based on AMP and Medicaid rebate data, the revisions to the Medicaid rebate formula and AMP definition described above could cause the required 340B discount to increase.

Effective in 2011, ACA imposed a requirement on manufacturers of branded drugs and biologic products to provide a discount off the negotiated price of branded drugs dispensed to Medicare Part D patients in the coverage gap (the "donut hole"). Moreover, the Bipartisan Budget Act of 2018 also amended the ACA, effective January 1, 2019, by increasing the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and closing the coverage gap.

Effective in 2011, ACA imposed an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic products, apportioned among these entities according to their market share in certain government healthcare programs, although this fee would not apply to sales of certain products approved exclusively for orphan indications.

As part of efforts to further transparency of payments made by pharmaceutical companies to physicians, ACA required manufacturers to track certain financial arrangements with physicians and teaching hospitals, including any "transfer of value" made or distributed to such entities, as well as any investment interests held by physicians and their immediate family members. Manufacturers were required to begin reporting this information to CMS beginning in 2014. Annual reporting is required, and records of payments are publicly available for review on the CMS website.

As of 2010, a new Patient-Centered Outcomes Research Institute was established pursuant to ACA to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research. The research conducted by the Patient-Centered Outcomes Research Institute may affect the market for certain pharmaceutical products.

The ACA created the Independent Payment Advisory Board, or IPAB, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription drugs. However, the IPAB implementation has been not been clearly defined. ACA provided that under certain circumstances, IPAB recommendations will become law unless Congress enacts legislation that will achieve the same or greater Medicare cost savings.

The ACA established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Anti-Kickback Laws

United States federal laws, including the federal Anti-Kickback Statute, prohibit fraud and abuse involving state and federal healthcare programs, such as Medicare and Medicaid. These laws are interpreted broadly and enforced aggressively by various federal agencies, including CMS, the Department of Justice, and the Office of Inspector General for the United States Department of Health and Human Services (HHS) and various state agencies. These anti-kickback laws prohibit, among other things, any person from knowingly and willfully offering, paying, soliciting, receiving, or providing remuneration, directly or indirectly, in exchange for or to induce either the referral of an individual, or the furnishing, arranging for, or recommending of an item or service that is reimbursable, in whole or in part, by a federal healthcare program. Remuneration is broadly defined to include anything of value, such as cash payments, gifts or gift certificates, discounts, or the furnishing of services, supplies, or equipment. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other. The anti-kickback laws are broad and prohibit many arrangements and practices that are lawful in businesses outside of the healthcare industry. A person or entity need not have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it in order to have committed a violation.

The penalties for violating the anti-kickback laws can be severe. The sanctions include criminal and civil fines and penalties for each violation, plus imprisonment and possible exclusion from the federal healthcare programs. In addition, the government may assert that a claim that includes items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution. Many states have adopted laws similar to the federal anti-kickback laws, and some apply to items and services reimbursable by any payor, including third-party payors.

Federal and State Prohibitions on False Claims

The federal False Claims Act imposes liability on any person or entity that, among other things, knowingly presents, or causes to be presented, a false, fictitious or fraudulent claim for payment to, or approval by, the federal government or knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim or obligation to pay or transmit money or property to the federal government, or knowingly and improperly avoiding or decreasing an obligation to pay money to the federal government. Under the False Claims Act, a person acts knowingly if he has actual knowledge of the information or acts in deliberate ignorance or in reckless disregard of the truth or falsity of the information. The government may deem manufacturers to have caused the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customers or promoting a product off-label. Companies that submit claims directly to payors may also be liable under the False Claims Act for the direct submission of such claims. In addition, our future activities relating to the reporting of wholesaler or estimated retail prices for our products, the reporting of prices used to calculate Medicaid rebate information and other information affecting federal, state, and third-party reimbursement for our products, and the sale and marketing of our products, are subject to scrutiny under this law.

Actions under the False Claims Act may be brought by the Attorney General or as a qui tam action by a private individual on behalf of the federal government who shares in any amounts paid by the defendant to the government in connection with the action. The number of filings under these provisions has increased significantly in recent years. Conduct that violates the False Claims Act may also lead to exclusion from the federal healthcare programs. Further, violations of the False Claims Act can result in very significant monetary penalties and treble damages. In addition, the civil monetary penalties statute imposes penalties against any person who is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent. Many states have enacted similar laws modeled after the False Claims Act that apply to items and services reimbursed under Medicaid and other state healthcare programs, and, in several states, such laws apply to claims submitted to all payors. Given the significant size of actual and potential settlements, it is expected that the government authorities will continue to devote substantial resources to investigating healthcare providers' and manufacturers' compliance with applicable fraud and abuse laws.

Federal Prohibitions on Healthcare Fraud and False Statements Related to Healthcare Matters

The federal Health Insurance Portability and Accountability Act of 1996 (HIPAA) created new federal criminal statutes that prohibit, among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the United States Federal Anti-Kickback Statute, ACA broadened the reach of certain criminal healthcare fraud statutes created under HIPAA by amending the intent requirement such that a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

Health Insurance Portability and Accountability Act

We may also be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act (HITECH), and their respective implementing regulations, including the final omnibus rule published on January 26, 2013, impose specified requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates that perform services for them that involve the use, or disclosure of, individual identifiable health information, relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to "business associates," defined as independent contractors or agents of covered entities that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, there may be additional federal, state, and non-U.S. laws which govern the privacy and security of health and other personal information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Furthermore, international laws, such as the EU Data Privacy Directive (95/46/EC) and Swiss Federal Act on Data Protection, regulate the processing of personal data within Europe and between European countries and the United States. Failure to provide adequate privacy protections and maintain compliance with safe harbor mechanisms could jeopardize business transactions across borders and result in significant penalties.

Physician Payments Sunshine Act

There has been a recent trend of increased federal and state regulation of payments made to physicians and other healthcare providers. The Physician Payments Sunshine Act requires most pharmaceutical manufacturers to report annually to the Secretary of HHS, under the Open Payments Program, information regarding any payments or other "transfers of value" made or distributed by that entity to physicians (defined to include doctors, dentists, optometrists, podiatrists, and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Over the next several years, we will need to dedicate significant resources to establish and maintain systems and processes in order to comply with these regulations. Failure to submit required information may result in civil monetary penalties for all payments, transfers of value or ownership or investment interests that are not timely, accurately, and completely reported in an annual submission. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made to certain non-physical providers such as physician assistants and nurse practitioners. In addition, certain states require implementation of compliance programs and compliance with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, impose restrictions on marketing practices, and/or tracking and reporting of gifts, compensation and other remuneration or items of value provided to physicians and other healthcare professionals and entities. Similar laws have been enacted or are under consideration in foreign jurisdictions, including France which has adopted the Loi Bertrand, or French Sunshine Act, which became effective in 2013, and Belgium which enacted their Sunshine Act in 2016.

Non-U.S. Healthcare Laws

To the extent that any of our product candidates, once approved, are sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or other transfers of value to healthcare professionals, and data privacy and security laws and regulations in foreign jurisdictions that may be more stringent than those in the United States (such as the European Union, which adopted the General Data Protection Regulation, or GDPR, which became effective in May 2018). In addition to U.S. regulations, we are subject to regulations of other countries governing clinical trials and distribution of our products outside of the United States. Regardless of FDA status for a product, we must obtain approval by the comparable regulatory authorities of countries outside of the U.S. before we can commence clinical trials in such countries. The approval process and requirements governing the conduct of clinical trials vary greatly from place to place, and the time may be longer or shorter than that required for FDA approval.

Regulations Governing Data Collection and the Use, Processing and Cross-Border Transfer of Personal Information

We have conducted, and may continue to conduct, clinical trials or continue to enroll subjects in our ongoing or future clinical trials in certain jurisdictions in which we may be subject to additional privacy restrictions. The collection, use, storage, disclosure, transfer, or other processing of personal data regarding individuals in the EU, including personal health data, is subject to the GDPR, which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the EU, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR includes restrictions on cross-border data transfers. The GDPR may increase our responsibility and liability in relation to personal data that we process where such processing is subject to the GDPR, and we may be required to put in place additional mechanisms to ensure compliance with the GDPR, including as implemented by individual countries. Compliance with the GDPR will be a rigorous and time-intensive process that may increase our cost of doing business or require us to change our business practices, and despite those efforts, there is a risk that we may be subject to fines and penalties, litigation, and reputational harm in connection with our European activities. Further, the United Kingdom's vote in favor of exiting the EU, often referred to as Brexit, has created uncertainty with regard to data protection regulation in the United Kingdom. In particular, it is unclear how data transfers to and from the United Kingdom will be regulated.

California recently enacted the California Consumer Privacy Act (CCPA), which creates new individual privacy rights for California consumers (as defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. The CCPA will require covered companies to provide certain disclosures to consumers about its data collection, use and sharing practices, and to provide affected California residents with ways to opt-out of certain sales or transfers of personal information. The CCPA went into effect on January 1, 2020, and the California Attorney General will commence enforcement actions against violators beginning July 1, 2020. While there is currently an exception for protected health information that is subject to HIPAA and clinical trial regulations as currently written, the CCPA may impact our business activities. The California Attorney General has proposed draft regulations, which have not been finalized to date, that may further impact our business activities if they are adopted. The uncertainty surrounding the implementation of CCPA exemplifies the vulnerability of our business to the evolving regulatory environment related to personal data and protected health information.

Healthcare Reform and Regulatory Changes

The United States and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system that could affect our ability to profitably sell our products. In the United States, there have been and continue to be laws enacted by the federal government, state governments, regulators and third-party payers to control healthcare costs, and generally, to reform the healthcare system in the United States.

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medical products. By way of example, in the United States, the Medicare Prescription Drug Improvement and Modernization Act of 2003 (MMA), changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for outpatient drug purchases by those covered by Medicare under a new Part D and introduced a new reimbursement methodology based on average sales prices for Medicare Part B physician-administered drugs. As a result of this legislation and the expansion of federal coverage of drug products, there is additional pressure to contain and reduce costs. While the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates, and any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payors.

In addition, in March 2010, ACA was enacted, which, among other things, increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, extended the Medicaid Drug Rebate Program to utilization of prescriptions of individuals enrolled in Medicaid managed care plans, imposed mandatory discounts for certain Medicare Part D beneficiaries, and subjected drug manufacturers to new annual fees based on pharmaceutical companies' share of sales to federal healthcare programs.

On August 2, 2011, the Budget Control Act of 2011 created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This included aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments, will remain in effect through 2029 unless additional Congressional action is taken. On January 2, 2013, the American Tax Payer Relief Act was signed into law, which, among other things, further reduced Medicare payments to several providers, including hospitals.

Some of the provisions of the ACA have yet to be fully implemented, while certain provisions have been subject to judicial and Congressional challenges. Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the ACA have been signed into law. The Tax Cuts and Jobs Act of 2017 (the Tax Act), includes a provision that decreased the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year, commonly referred to as the "individual mandate," to $0 effective January 1, 2019. On December 14, 2018, a federal district court in Texas ruled the individual mandate is a critical and inseverable feature of the ACA, and therefore, because it was repealed as part of the Tax Act, the remaining provisions of the ACA are invalid as well. On December 18, 2019, the Fifth Circuit U.S. Court of Appeals held that the individual mandate is unconstitutional and remanded the case to the lower court to reconsider its earlier invalidation of the full ACA. Pending review, the ACA remains in effect, but it is unclear at this time what effect the latest ruling will have on the status of the ACA.

Since January 2017, President Trump has signed two Executive Orders and other directives designed to delay the implementation of certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. On January 20, 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On October 13, 2017, President Trump signed an Executive Order terminating the cost-sharing subsidies that reimburse insurers under the ACA. The Trump administration has concluded that cost-sharing reduction (CSR) payments to insurance companies required under the ACA have not received necessary appropriations from Congress and announced that it will discontinue these payments immediately until those appropriations are made. The loss of the CSR payments is expected to increase premiums on certain policies issued by qualified health plans under the ACA. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. The Bipartisan Health Care Stabilization Act of 2017, as well as the follow-on Bipartisan Health Care Stabilization Act of 2018 were introduced to appropriate funds to stabilize CSR payments; however, the future of this effort is unclear. On June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12 billion in ACA risk corridor payments to third-party payors who argued were owed to them. The effects of this gap in reimbursement on third-party payors, the viability of the ACA marketplace, providers, and potentially our business, are not yet known. In December 2018, CMS published a final rule permitting further collections and payments to and from certain ACA qualified health plans and health insurance issuers under the ACA risk adjustment program in response to the outcome of the federal district court litigation regarding the method CMS uses to determine this risk adjustment. In addition, CMS published a final rule that would give states greater flexibility, starting in 2020, in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces.

On January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called “Cadillac” tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices; however, on December 20, 2019, President Trump signed into law the Further Consolidated Appropriations Act (H.R. 1865), which repeals the Cadillac tax, the health insurance provider tax, and the medical device excise tax. It is impossible to determine whether similar taxes could be instated in the future. Moreover, the Bipartisan Budget Act of 2018, among other things, amends the ACA, effective January 1, 2019 by increasing the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and closing the coverage gap in most Medicare drug plans, commonly referred to as the “donut hole.”

The full impact of the ACA, any law repealing, replacing, or modifying elements of it, and the political uncertainty surrounding its repeal, replacement, or modification on our business remains unclear. We expect that additional federal healthcare reform measures may be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare drugs and services.

There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At the federal level, the Trump administration’s budget proposal for fiscal years 2019 and 2020 contain further drug price control measures that could be enacted during the budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. Additionally, the Trump administration released a “Blueprint” to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. The U.S. Department of Health and Human Services has already started the process of soliciting feedback on some of these measures and, at the same time, is immediately implementing others under its existing authority. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage Plans the option of using step therapy, a type of prior authorization, for Part B drugs beginning January 1, 2020. This final rule codified CMS’s policy change that was effective January 1, 2019. Although a number of these, and other proposed measures may require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

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

Employees

As of December 31, 2019, we had 235 full-time employees. Our employees are not represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Facilities

Information regarding our facilities is included in Note 6 “Leases” of the footnotes to the consolidated financial statements included in this Annual Report on Form 10-K.

We use various trademarks and trade names in our business, including without limitation our corporate name and logo. All other trademarks or trade names, including without limitation corporate names and logos, referred to in this report are the property of their respective owners. Solely for convenience, the trademarks and trade names in this report may be referred to without the ® and ™ symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

Available Information

We post our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and any exhibits or amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, on the Investors & Media section of our public website (www.myokardia.com, accessible to you free of charge), as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. In addition, you can read our SEC filings over the Internet at the SEC’s website at www.sec.gov. The contents of these websites are not incorporated into this Annual Report on Form 10-K. Further, our references to the URLs for these websites are intended to be inactive textual references only. We do not incorporate the information on or accessible through our website into this Annual Report on Form 10-K, and you should not consider any information on, or that can be accessed through, our website a part of this Annual Report on Form 10-K.

Item 1A. RISK FACTORS

You should consider carefully the following risk factors, together with all the other information in this report, including our consolidated financial statements and notes thereto, and in our other public filings with the SEC. The occurrence of any of the following risks could harm our business, financial condition, results of operations and/or growth prospects or cause our actual results to differ materially from those contained in forward-looking statements we have made in this report and those we may make from time to time. You should consider all of the risk factors described when evaluating our business.

Risks Related to Our Precision Medicine Platform and the Discovery and Development of Our Product Candidates

The precision medicine approach we are taking to discover and develop drugs for serious diseases of systolic or diastolic dysfunction is novel and may never lead to marketable products.

We have concentrated our therapeutic product research and development efforts on the application of precision medicine to the treatment of cardiovascular diseases, and our future success depends on the successful development of products based on our precision medicine platform and the continued development of this platform. We believe we are the first company to apply precision medicine to the treatment of cardiovascular disease, and neither we nor any other company has received regulatory approval to market therapeutics specifically targeting the underlying cause of cardiomyopathy. The scientific discoveries that form the basis for our efforts to discover and develop product candidates are novel, and the scientific evidence to support the feasibility of developing product candidates based on these discoveries is both preliminary and limited. If we do not successfully develop and commercialize product candidates based upon our technological approach, we will not become profitable and the value of our common stock may decline.

Further, our focus, which has been solely on precision medicine for the development of drugs for diseases of cardiac muscle contraction as opposed to multiple, more proven technologies for drug development, increases the risks associated with the ownership of our common stock. If we are not successful in developing any product candidates using our precision medicine platform, we may be required to change the scope and direction of our product development activities. In that case, we may not be able to identify and implement successfully an alternative product development strategy, which would materially and adversely affect our business, financial condition and results of operations.

We depend heavily on the success of mavacamten, danicamtiv and MYK-224, our initial product candidates. Other than mavacamten, danicamtiv and MYK-224, all of our other programs are in discovery or preclinical development. Preclinical testing and clinical trials of our product candidates may not be successful. If we are unable to commercialize our product candidates or experience significant delays in doing so, our business will be materially harmed.

We have invested a significant portion of our efforts and financial resources in the identification of our initial product candidates, mavacamten and MYK-224 for the treatment of hypertrophic cardiomyopathy (HCM) and danicamtiv for the treatment of dilated cardiomyopathy (DCM). We are currently evaluating mavacamten, danicamtiv and MYK-224 in clinical trials, and, if these product candidates fail to demonstrate safety or efficacy in their respective target indications to the satisfaction of the FDA or other comparable regulatory authorities, we will need to identify and rely on other product candidates or target indications, or both, for clinical development. All of our other programs are still in discovery or preclinical development. Our ability to generate revenue from product sales, which we do not expect will occur for years, if ever, will depend heavily on the successful development and eventual commercialization of mavacamten, danicamtiv, MYK-224 or other product candidates that we may identify from our precision medicine platform.

The success of mavacamten, danicamtiv, MYK-224 and any other product candidates that we discover and develop will depend on many factors, including the following:

- timely and successful initiation of, enrollment in, and completion of, clinical trials, including our Phase 3 clinical trial of mavacamten in HCM, our Phase 2 clinical trial of danicamtiv in genetic DCM, our Phase 1 clinical trial of MYK-224 and any additional clinical trials of these product candidates;
- achieving positive safety and efficacy data and desirable medicinal properties for our product candidates for the intended indications;
- our ability to receive, and the timing of our receipt of, any marketing approvals from applicable regulatory authorities;
- establishing and maintaining manufacturing capabilities or making arrangements with third-party manufacturers for the manufacture of our product candidates for clinical trials and, if approved, for commercialization;
- obtaining and maintaining patent and trade secret protection and non-patent exclusivity for our product candidates;
- launching commercial sales of our products, if and when approved, whether alone or in collaboration with others;
- acceptance of our products, if and when approved, by patients, the medical community and third-party payors;

- effectively competing with other therapies;
- a continued acceptable safety profile of our products following approval; and
- enforcing and defending intellectual property rights and claims.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our product candidates, which would materially harm our business.

Preclinical and clinical drug development involves a lengthy and expensive process with an uncertain outcome, and observations and results from earlier studies and trials may not be applicable or predictive in future clinical trials.

Preclinical and clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the preclinical development or clinical trial process. The results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. For example, although our preclinical observations and data generated from our Phase 1 and Phase 2 clinical trials of mavacamten support our hypothesis that mavacamten has the potential to reduce cardiac muscle contractility and our belief that such data have demonstrated clinical proof of mechanism in both HCM patients and healthy volunteers, we have not completed placebo controlled clinical trials of mavacamten in larger populations using the current dosing strategy, inclusion/exclusion criteria, and endpoints of EXPLORER-HCM. In addition, our precision medicine platform is based on a translational medicine approach. Translational medicine, or the application of basic scientific findings to develop therapeutics that promote human health, is subject to a number of inherent risks. In particular, scientific hypotheses formed from preclinical or early clinical observations may prove to be incorrect, and the data generated in animal models or observed in limited patient populations may be of limited value and may not be applicable in clinical trials conducted under the controlled conditions required by applicable regulatory requirements and our protocols. The initial clinical data from our Phase 1 and Phase 2 clinical trials of mavacamten, as well as our Phase 1 and 2 clinical trials of danicamtiv, are preliminary in nature, and the clinical development of mavacamten and danicamtiv is not complete. Early positive data may not be repeated or observed in ongoing or future trials involving our product candidates. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. There is a high failure rate for drugs and biologics proceeding through clinical trials, particularly in the field of cardiovascular medicine. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in clinical development even after achieving promising results in earlier studies, and any such setbacks in our clinical development could have a material adverse effect on our business and operating results.

We may encounter substantial delays in our clinical trials or we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidates in humans. Clinical testing is expensive, time-consuming and uncertain as to outcome. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. A failure of one or more clinical trials can occur at any stage of testing. We may experience delays in our ongoing clinical trials and we do not know whether planned clinical trials will begin on time, need to be redesigned, enroll patients on time or be completed on schedule, if at all. Additionally, although we believe that our precision medicine approach should eliminate the need for mavacamten to undergo the large outcomes-based studies that are often required for cardiovascular drugs as a condition to regulatory approval by the FDA or other regulatory authorities, regulatory authorities may nevertheless require us to conduct additional trials or generate additional data, including potential trials studying the interaction of our product candidates with other therapeutics commonly administered in the patient populations we are seeking to treat, which would increase the time and cost of our clinical development process. Furthermore, we will need to conduct larger clinical trials, and the FDA may subsequently require us to evaluate a larger number of patients than we presently anticipate, or to assess other endpoints besides those presently contemplated, in order to support regulatory approval.

Clinical trials can be delayed for a variety of reasons, including:

- delays in reaching a consensus with regulatory agencies on trial design;
- delays in reaching agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- delays in obtaining required Institutional Review Board (IRB) approval at each clinical trial site;
- delays in recruiting suitable patients to participate in our clinical trials;
- imposition of a clinical hold by regulatory agencies, including after an inspection of our clinical trial operations or trial sites;

- failure by our CROs, other third parties or us to adhere to clinical trial requirements;
- failure by us, our CROs or other third-party contractors to perform clinical trials in accordance with the FDA's good clinical practice (GCP) requirements or applicable regulatory guidelines in other countries;
- delays in the testing, validation, manufacturing and delivery of our product candidates to the clinical sites;
- delays in having patients complete participation in a study or return for post-treatment follow-up;
- clinical trial sites deviating from a trial protocol or dropping out of a trial;
- clinical trial subjects failing to comply with the trial regimen or dropping out of a trial;
- adding new clinical trial sites;
- failure to manufacture or supply sufficient quantities of product candidates for use in clinical trials;
- occurrence of serious adverse events associated with the product candidate that are viewed to outweigh its potential benefits; or
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols.

We could encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, or suspension or termination is recommended by the Data Safety Monitoring Board for such trial or by the FDA or other regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or other regulatory authorities. The FDA or other regulatory authorities may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA or other regulatory authorities may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or other regulatory authorities, as the case may be, and may ultimately lead to the denial of marketing approval of one or more of our product candidates.

Any inability to successfully complete preclinical and clinical development could result in additional costs to us or impair our ability to generate revenues from product sales, and, if applicable under any collaboration or similar agreement, regulatory and commercialization milestones and royalties. In addition, if we make manufacturing or formulation changes to our product candidates, we may need to conduct additional studies to bridge our modified product candidates to earlier versions. Clinical trial delays could also shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may harm our business and results of operations. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

If the results of our clinical trials are inconclusive or if there are safety concerns or adverse events associated with our product candidates, we may:

- be delayed in obtaining marketing approval for our product candidates, if at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant restrictions on use or distribution of the drug;
- require safety warnings in the label and/or require risk management plan post-approval;
- be required to perform additional clinical trials to support approval or be subject to additional post-marketing testing requirements;
- have regulatory authorities withdraw their approval of the product or impose restrictions on its distribution in the form of a modified risk evaluation and mitigation strategy (REMS);
- be subject to the addition of labeling statements, such as warnings or contraindications;

- be sued; or
- experience damage to our reputation.

We may find it difficult to enroll patients in our clinical trials, which could delay or prevent clinical trials of our product candidates.

Identifying and qualifying patients to participate in clinical trials of our product candidates is critical to our success. The timing to commence and complete our clinical trials depends on the speed at which we can recruit patients to participate in testing our product candidates. If patients are unwilling to participate in our clinical trials because of a lack of familiarity with our approach to the treatment of cardiovascular diseases, negative publicity from adverse events in biotechnology or the fields of precision medicine or cardiovascular disease or for other reasons, including competitive clinical trials for similar patient populations, our timelines for recruiting patients, conducting clinical trials and obtaining regulatory approval of potential products may be delayed. These delays could result in increased costs, delays in advancing our product development, delays in testing the effectiveness of our product candidates or termination of our clinical trials altogether.

We may not be able to identify, recruit and enroll a sufficient number of patients, or those with required or desired characteristics to achieve diversity in a study, to complete our clinical trials in a timely manner. Patient enrollment is affected by factors including:

- severity of the disease under investigation;
- design of the clinical trial protocol;
- size and nature of the patient population;
- eligibility criteria for the clinical trial in question;
- perceived risks and benefits of the product candidate under study in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating;
- proximity and availability of clinical trial sites for prospective patients;
- availability of competing therapies and clinical trials;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians; and
- ability to monitor patients adequately during and after treatment.

In particular, each of the conditions in which we are evaluating or plan to evaluate our product candidates are rare genetic disorders or involve segmented patient populations with limited patient pools from which to draw for clinical trials. To date, the HCM and DCM patient populations have not been extensively evaluated in clinical trials. As a result, enrollment in our ongoing and planned clinical trials is difficult to predict and may take longer or cost more than we anticipate.

We plan to seek initial marketing approval in the United States. We may not be able to initiate or continue clinical trials if we cannot enroll a sufficient number of eligible patients to participate in the clinical trials required by the FDA or other regulatory agencies. Our ability to successfully initiate, enroll and complete a clinical trial in any foreign country is subject to numerous risks unique to conducting business in foreign countries, including:

- difficulty in establishing or managing relationships with CROs and physicians;
- different standards for the conduct of clinical trials;
- our inability to locate qualified local consultants, physicians and partners; and
- the potential burden of complying with a variety of foreign laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatment.

If we have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay, limit or terminate ongoing or planned clinical trials, any of which would have an adverse effect on our business.

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

The success of our business depends primarily upon our ability to identify, develop and commercialize therapeutics for the treatment of cardiovascular diseases based on our precision medicine approach. A key element of our initial strategy is to use our precision medicine platform to identify and study compounds that can be used to correct or offset the abnormal contraction caused by HCM and DCM. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for a number of reasons, including:

- the research methodology used may not be successful in identifying appropriate biomarkers or potential product candidates;
- our initial hypotheses based on our preclinical or early clinical observations may not be supported by later clinical results;
- potential product candidates may, on further study, be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval; or
- research programs to identify new product candidates require substantial technical, financial and human resources. We may choose to focus our efforts and resources on a potential product candidate that ultimately proves to be unsuccessful.

If we are unable to identify suitable compounds for preclinical and clinical development, we may be forced to abandon our development efforts for a research program or programs and we will not be able to obtain product revenues in future periods, which likely would result in significant harm to our financial position and adversely impact our stock price.

Any of our product candidates may cause adverse effects or have other properties that could delay or prevent their regulatory approval, limit the scope of any approved label or market acceptance or result in other significant negative consequences following marketing approval, if any.

Adverse events or other unintended side effects or safety signals caused by our product candidates could cause us, IRBs or ethics committees, clinical trial sites or regulatory authorities to interrupt, delay or halt clinical trials and could result in the denial of regulatory approval. For example, through additional studies, we may determine that although mavacamten has been shown to be specific to striated muscle, which includes both skeletal and cardiac muscle, and selective for cardiac muscle, it may target myosin in skeletal muscle, which could result in unintended adverse effects.

We have observed adverse events in our clinical trials of mavacamten. Results of our ongoing and planned trials could reveal a high and unacceptable severity and prevalence of these or other adverse events in subjects treated with our product candidates. Additionally, if the adverse events we have observed are deemed to be unacceptable or other unacceptable side effects or safety signals are observed in any ongoing or subsequent preclinical studies or clinical trials of our product candidates, our trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. Any adverse effects encountered in our preclinical studies or clinical trials, whether or not drug-related, could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Additionally, adverse effects may represent safety signals that could influence the benefit-risk assessment for further development or commercialization of a product candidate and may warrant further clinical or nonclinical investigation, consultation with health authorities, changes to product labeling or guidelines for its safe use, or other scientific or regulatory actions. Any of these occurrences may harm our business, financial condition and prospects significantly.

Further, if any of our future products, if and when approved for commercial sale, cause serious or unexpected adverse events, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw their approval of the product or impose restrictions on its distribution in the form of a REMS or provide a medication guide outlining the risks of such side effects for distribution to patients;
- regulatory authorities may require the addition of labeling statements, such as warnings or contraindications;
- we may be required to change the way the product is administered or conduct additional clinical trials;
- we could be sued and held liable for harm caused to patients; or
- our reputation may suffer.

Any of these events could prevent us or our partners from achieving or maintaining market acceptance of the affected product and could substantially increase the costs of commercializing our future products and impair our ability to generate revenues from the commercialization of these products.

Risks Related to Government Regulation

We currently do not have regulatory approval to market any of our product candidates. The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our product candidates, our business will be substantially harmed.

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

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

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;
- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of a New Drug Application (NDA) or other submission or to obtain regulatory approval in the United States or elsewhere;
- the FDA or comparable foreign regulatory authorities may find deficiencies with or fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; or
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

This lengthy approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market mavacamten, danicamtiv or any other product candidate we may develop, which would significantly harm our business, results of operations and prospects.

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

Although the FDA provided feedback on the Phase 3 clinical trial for mavacamten, the FDA may raise questions regarding mavacamten's safety data, which may delay or prevent the approval of mavacamten or adversely affect our ability to commercialize mavacamten on the timelines we have announced.

The size of a safety database when submitting an NDA is usually between 3,000 to 5,000 patients. When we sought feedback on EXPLORER-HCM, our Phase 3 clinical trial for mavacamten, we estimated that at the time of submitting our NDA, our safety database would have 250 patient-years of exposure, as we are treating an orphan disease. When we submit our NDA, we anticipate that we will have approximately 200 patient-years in the safety database and at the time of submission of the 120-day safety update, it will have increased to 300-350 patient-years. While we plan to conduct a prospective registry study to demonstrate our commitment to post-approval product characterization, and the FDA has accepted a lesser number of patients for a safety database in the past, the FDA may request additional clinical data, which may delay or prevent the approval and commercialization of mavacamten and could have a negative impact on our business.

Even if we complete the necessary preclinical studies and clinical trials, we cannot predict when or if we will obtain regulatory approval to commercialize a product candidate or the approval may be for a more limited indication than we expect.

We cannot commercialize a product until the appropriate regulatory authorities have reviewed and approved the product candidate. Even if our product candidates demonstrate safety and efficacy in clinical trials, the regulatory agencies may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval. Additional delays may result if an FDA Advisory Committee or other regulatory authority recommends non-approval or restrictions on approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory agency policy during the period of product development, clinical trials and the review process. Regulatory agencies also may approve a treatment candidate for fewer or more limited indications than requested or may grant approval subject to the performance of post-marketing studies. In addition, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of our treatment candidates. If we are unable to obtain regulatory approval for our product candidates for use in the treatment of cardiomyopathies, our business may suffer.

Failure to obtain marketing approval in international jurisdictions would prevent our products from being marketed in such jurisdictions.

In order to market and sell our products in the European Union and many other jurisdictions, we or any third-party collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We or these third parties may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. However, the failure to obtain approval in one jurisdiction may negatively impact our ability to obtain approval in other jurisdictions. We may not be able to file for marketing approvals, and even if we do, we may not obtain necessary approvals to commercialize our medicines in any market.

Even if we receive regulatory approval for any of our product candidates, we will be subject to ongoing obligations and continued regulatory review, which may result in significant additional expense. Additionally, our product candidates, if approved, could be subject to labeling and other restrictions and market withdrawal and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products.

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to extensive and ongoing regulatory requirements and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, current Good Manufacturing Practice (cGMP) requirements relating to quality control, quality assurance and corresponding maintenance of records and documents, and requirements regarding the distribution of samples to physicians and recordkeeping. For example, the holder of an approved NDA is obligated to monitor and report adverse events and any failure of a product to meet the specifications in the NDA. The holder of an approved NDA must also submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process.

In addition, product manufacturers and their facilities are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP and adherence to commitments made in the NDA and other marketing authorizations.

Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval or contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the medicine.

The FDA closely regulates the post-approval marketing and promotion of medicines to ensure that they are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and if we do not market our medicines for their approved indications, we may be subject to enforcement action for off-label marketing.

In addition, later discovery of previously unknown problems with our medicines, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in various negative consequences, including:

- restrictions on the labeling, marketing or manufacturing of the product;
- restrictions on distribution or use of the product;
- requirements to conduct post-marketing clinical trials or holds on ongoing or planned clinical trials;
- warning or untitled letters;
- withdrawal of the medicines from the market;
- refusal by the FDA or comparable foreign regulatory authorities to approve pending applications or supplements to approved applications that we submit;
- mandatory or voluntary recalls;
- fines, restitution or disgorgement of profits or revenue;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of our medicines;
- product seizure or detention; and
- injunctions or the imposition of civil or criminal penalties.

The FDA's policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

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

We may seek one or more special designations from regulatory authorities to expedite the review and approval process for our product candidates, including Breakthrough Therapy Designation or Fast Track Designation. These designations may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that our product candidates will receive marketing approval.

We may seek one or more special designations from regulatory authorities to expedite the review and approval process for our product candidates, including Breakthrough Therapy Designation or Fast Track Designation.

A breakthrough therapy is defined as a product that is intended, alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically important endpoints, such as substantial treatment effects observed early in clinical development. For products that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Products designated as breakthrough therapies by the FDA can also be eligible for accelerated approval. If a product is intended for the treatment of a serious or life-threatening condition and the product demonstrates the potential to address unmet medical needs for this condition, the product sponsor may apply for Fast Track Designation.

The FDA has broad discretion whether or not to grant these designations, so even if we believe a particular product candidate is eligible for a particular designation, we cannot assure you that the FDA would decide to grant it. Accordingly, even if we believe one of our product candidates meets the criteria for a designation, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a particular designation for a product candidate may not result in a faster development process, review or approval compared to products considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that the products no longer meet the conditions for qualification and rescind the breakthrough designation. Further, the FDA may withdraw Fast Track Designation if it believes that the designation is no longer supported by data from a clinical development program.

If we elect to pursue Breakthrough Therapy Designation or Fast Track Designation, any inability to secure or maintain the applicable designation would have an adverse impact on our development timelines and our ability to obtain approval for and commercialize our product candidates.

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

Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

We are an early-stage company. We were incorporated and commenced operations in June 2012. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, developing our technology, creating and expanding on our precision medicine platform, identifying potential product candidates, undertaking preclinical studies for our programs, completing our ongoing clinical trials for our most advanced product candidate, mavacamten, planning further clinical development of mavacamten and completing our ongoing clinical development of our second product candidate, danicamtiv, and beginning clinical development of our third product candidate, MYK-224. We have not yet demonstrated our ability to successfully complete the clinical development of a product candidate, including the completion of any clinical trials designed to support the registration of a product candidate, obtain marketing approvals, manufacture a commercial scale medicine, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful commercialization. Typically, it takes many years to develop a new medicine from the time it is discovered to when it is available for treating patients. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

In addition, as a new business, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will need to transition from a company with a research and development focus to a company capable of supporting larger scale clinical development and commercial activities. If we are not successful in such a transition, our business, results and financial condition will be harmed.

We have a history of significant losses and anticipate that we will continue to incur losses for the near future and may not achieve or sustain profitability and, as a result, you may lose all or part of your investment.

Our initial product candidates, mavacamten, danicamtiv and MYK-224, are in various stages of clinical testing and we must successfully complete our ongoing clinical trials of mavacamten and conduct significant additional clinical trials for danicamtiv and MYK-224 before we can seek the regulatory approvals necessary to begin commercial sales of these or any other product candidates we may develop. We have incurred operating losses in each year since our inception due to costs incurred in connection with our research and development activities and selling, general and administrative costs associated with our operations. Our net loss for the year ended December 31, 2019 was $287.8 million and as of December 31, 2019, we had an accumulated deficit of $478.8 million. We expect to incur increasing losses for several years as we continue our research activities and conduct development of, and seek regulatory approvals for, our initial product candidates, and commercialize any approved drugs. If our product candidates fail in clinical trials or do not gain regulatory approval, or if our product candidates do not achieve market acceptance, we will not be profitable. If we fail to become and remain profitable, or if we are unable to fund our continuing losses, you could lose all or part of your investment.

We have never generated any revenue from product sales and may never be profitable.

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

- completing research and preclinical and clinical development of our product candidates;
- seeking and obtaining regulatory approvals to market product candidates for which we complete clinical trials;
- developing a sustainable, scalable, reproducible and transferable manufacturing process for our product candidates;
- establishing and maintaining supply and manufacturing relationships with third parties that can provide adequate (in amount and quality) products and services to support clinical development and the market demand, if any, for our product candidates, if approved;
- launching and commercializing product candidates for which we obtain regulatory approval, either through a collaboration or, if launched independently, by establishing a sales force, marketing and distribution infrastructure;

- obtaining market acceptance of our product candidates and the use of precision medicine as a viable treatment option for cardiovascular diseases;
- addressing any competing technological and market developments;
- implementing additional internal systems and infrastructure, as needed;
- identifying and validating new product candidates from our platform;
- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trade secrets and know-how; and
- attracting, hiring and retaining qualified personnel who are suitable to our culture and mission.

Even if one or more of the product candidates that we are developing is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Our expenses could increase beyond our expectations if we are required by the U.S. Food and Drug Administration (FDA), the European Medicines Agency (EMA) or other regulatory agencies, domestic or foreign, to perform clinical trials and other studies in addition to those that we currently anticipate. Even if we are able to generate revenues from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations.

We will need to raise additional funding, which may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate our product development efforts or other operations.

We are currently advancing mavacamten, danicamtiv and MYK-224, our initial product candidates, through clinical development, and conducting preclinical discovery and development activities in our other programs. Drug development is expensive, and we expect our research and development expenses to increase substantially in connection with our ongoing activities, particularly as we continue to advance our product candidates in clinical trials and identify additional product candidates from our pipeline for clinical development.

As of December 31, 2019, our cash, cash equivalents and investments (short-term and long-term) totaled $430.3 million. We intend to use our cash, cash equivalents and investments to fund the advancement of our mavacamten clinical development program, including our ongoing Phase 3 clinical trial in symptomatic oHCM patients, and our planned additional clinical trials of mavacamten and danicamtiv, our ongoing Phase 1 trial of MYK-224, our ongoing preclinical, discovery and research programs and the expansion of our platform, as well as for working capital and general corporate purposes. However, our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic and licensing arrangements or a combination of these approaches. In any event, we will require additional capital to obtain regulatory approval for, and to commercialize, mavacamten, danicamtiv, MYK-224 or any other product candidates we may identify and develop. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or if we have specific strategic considerations.

Our funding requirements and the timing of our need for additional capital are subject to change based on a number of factors, including:

- the rate of progress and the cost of our ongoing and planned clinical trials of mavacamten, danicamtiv and MYK-224;
- the number of product candidates that we intend to develop using our precision medicine platform;
- the costs of research and preclinical studies to support the advancement of other product candidates into clinical development;
- the timing of, and costs involved in, seeking and obtaining approvals from the FDA and comparable foreign regulatory authorities, including the potential by the FDA or comparable regulatory authorities to require that we perform more studies than those that we currently expect;
- the costs of preparing to manufacture mavacamten on a commercial scale, and to manufacture danicamtiv and MYK-224 for further clinical development;
- the costs of commercialization activities if mavacamten or any future product candidate is approved, including the formation of a sales force;
- the degree and rate of market acceptance of any products launched by us or our partners, if any;

- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;
- our need and ability to hire additional personnel;
- our ability to enter into and maintain collaboration, licensing, commercialization or other arrangements and the terms and timing of such arrangements; and
- the emergence of competing technologies or other adverse market developments.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would dilute all of our stockholders. The incurrence of indebtedness would result in increased fixed payment obligations and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through arrangements with collaborative partners or otherwise at a different stage than otherwise would be desirable and we may be required to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the commercialization of any product candidates or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially and adversely affect our business, financial condition and results of operations.

Our reported financial results may be adversely affected by changes in accounting principles generally accepted in the United States.

We prepare our financial statements in conformity with accounting principles generally accepted in the United States. These accounting principles are subject to interpretation by the Financial Accounting Standards Board (FASB) and the Securities and Exchange Commission (SEC). A change in these policies or interpretations could have a significant effect on our reported financial results, may retroactively affect previously reported results, could cause unexpected financial reporting fluctuations, and may require us to make costly changes to our operational processes and accounting systems.

Comprehensive tax reform bills could increase the tax burden on our orphan drug programs and adversely affect our business and financial condition.

In December 2017, the U.S. government enacted comprehensive tax legislation that includes significant changes to the taxation of business entities. These changes include, among others, (i) a permanent reduction to the corporate income tax rate, (ii) a partial limitation on the deductibility of business interest expense, (iii) a shift of the U.S. taxation of multinational corporations from a tax on worldwide income to a generally more territorial focused system (along with certain rules designed to prevent erosion of the U.S. income tax base) and (iv) a one-time tax on accumulated offshore earnings held in cash and illiquid assets, with the latter taxed at a lower rate.

Further, the recently enacted comprehensive tax legislation, among other things, reduces the orphan drug tax credit from 50% to 25% of qualifying expenditures. When and if we become profitable, this reduction in tax credits may result in an increased federal income tax burden on our orphan drug programs as it may cause us to pay federal income taxes earlier under the revised tax law than under the prior law and, despite being partially off-set by a reduction in the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, may increase our total federal tax liability attributable to such programs.

Notwithstanding the reduction in the corporate income tax rate, the overall impact of this tax reform is uncertain, and our business and financial condition could be adversely affected. In addition, it is uncertain if and to what extent various states will conform to this federal tax law.

We may choose not to develop a potential drug candidate, or we may suspend, deprioritize or terminate one or more discovery programs or pre-clinical drug candidates or programs.

At any time and for any reason, we may determine that one or more of our discovery programs or preclinical drug candidates or programs does not have sufficient potential to warrant the allocation of resources toward such program or drug candidate. Accordingly, we may choose not to develop a potential drug candidate or elect to suspend, deprioritize or terminate one or more of our discovery programs or preclinical drug candidates or programs. If we suspend, deprioritize or terminate a program or drug candidate in which we have invested significant resources, we will have expended resources on a program that will not provide a full return on our investment and may have missed the opportunity to have allocated those resources to potentially more productive uses, including existing or future programs or drug candidates.

Risks Related to Our Reliance on Third Parties

From the inception of our collaboration arrangement with Sanofi in August of 2014 and through December 31, 2018 we were substantially dependent upon Sanofi for the development and eventual commercialization of mavacamten, danicamtiv, and MYK-224. As a result of the termination of the arrangement, we may be unable to commercialize certain product candidates.

We have previously depended upon our license and collaboration agreement with Aventis Inc., a wholly-owned subsidiary of Sanofi S.A. (Sanofi), which we refer to as the Collaboration Agreement, for financial and scientific resources related to the clinical development and commercialization of product candidates under our mavacamten, MYK-224, danicamtiv and HCM-2 programs and for the manufacturing of danicamtiv. On December 31, 2018, Sanofi notified us of their intent to terminate the collaboration and as a result, reimbursement for our research and development collaboration on mavacamten and MYK-224 ended in the first half of 2019. In addition, Sanofi did not elect to continue with the danicamtiv and HCM-2 programs, and the collaboration with respect to such programs was deemed terminated as of December 31, 2018. As a result of the termination, the development of our product candidates previously subject to the Collaboration Agreement could be significantly delayed and may have a material adverse effect on our results of operations and financial condition.

We may enter into collaborations that place the development and commercialization of our product candidates outside our control, require us to relinquish important rights or may otherwise be on terms unfavorable to us, and if our collaborations are not successful, our product candidates may not reach their full market potential.

Our drug development programs and the potential commercialization of our drug candidates will require substantial additional cash to fund expenses. For some of our drug candidates, we may decide to collaborate with additional pharmaceutical and biotechnology companies for the development and potential commercialization of those drug candidates. We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject drug candidate, the costs and complexities of manufacturing and delivering such drug candidate to patients, the potential of competing drugs, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborator may also consider alternative drug candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our drug candidate. The terms of any additional collaborations or other arrangements that we may establish may not be favorable to us.

Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate additional collaborations on a timely basis, on acceptable terms or at all. If we are unable to do so, we may have to curtail the development of the drug candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our drug candidates or bring them to market and generate drug revenue. The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations. Disagreements between parties to a collaboration arrangement regarding clinical development and commercialization matters can lead to delays in the development process or commercializing the applicable drug candidate and, in some cases, termination of the collaboration arrangement. These disagreements can be difficult to resolve if neither of the parties has final decision-making authority. Collaborations with pharmaceutical or biotechnology companies and other third parties often are terminated or allowed to expire by the other party.

We expect to rely on third parties to conduct some or all aspects of our clinical trials, protocol development and research and development activities, and these third parties may not perform satisfactorily.

We currently rely on third parties to conduct our clinical trials and expect to continue to rely on third parties with respect to some or all aspects of our clinical trials, protocol development and research and development activities.

Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it could delay our product development activities. Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibility to ensure compliance with all required regulations and study protocols. For product candidates that we develop and commercialize on our own, we will remain responsible for ensuring that each of our preclinical studies and clinical trials are conducted in accordance with the study plan and protocols. We and our third-party contractors and CROs are required to comply with GCP regulations, which are regulations and guidelines enforced by the FDA, the Competent Authorities of the Member States of the European Economic Area (EEA), and comparable foreign regulatory authorities for all products in clinical development. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our third-party contractors or CROs fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, EMA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials complies with GCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process.

If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our studies in accordance with regulatory requirements or our stated study plans and protocols, we will be delayed in completing, or may not be able to complete, the preclinical and clinical studies required to support future Investigational New Drug Application (IND) submissions and approval of our product candidates. Any of these events could lead to clinical study delays or failure to obtain regulatory approval or impact our ability to successfully commercialize future products. Some of these events could be the basis for FDA action, including injunction, request for voluntary recall, seizure or total or partial suspension of production.

We contract with third parties for the manufacture of our product candidates for preclinical and clinical testing and expect to continue to do so for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates or medicines or that such supply will not be available to us at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not have, nor do we plan to acquire, any manufacturing facilities. We currently rely, and expect to continue to rely, on third-party manufacturers for the manufacture of our product candidates for preclinical and clinical testing and for the commercial supply of any of these product candidates for which we may obtain marketing approval. To date, we have obtained materials for mavacamten for our clinical trials from third-party manufacturers, and we intend to rely on third-party manufacturers for our planned Phase 2 and Phase 3 clinical development activities for mavacamten and for our Phase 2 and any subsequent clinical trials of danicamtiv. Due to the Sanofi Collaboration Agreement termination on December 31, 2018, we no longer rely on Sanofi for our danicamtiv supplies and have executed service agreements with other third-party manufacturers for the manufacturing of danicamtiv.

Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured the product candidates ourselves, including:

- the inability to negotiate or maintain manufacturing agreements with third parties under commercially reasonable terms;
- reduced control as a result of using third-party manufacturers for all aspects of manufacturing activities;
- reliance on the third party for regulatory compliance, quality assurance, and safety and pharmacovigilance reporting;
- the possible breach of the manufacturing agreement by the third party;
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us; and
- disruptions to the operations of our third-party manufacturers or suppliers caused by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier.

The facilities used by our contract manufacturers to manufacture any of our future products must be evaluated by the FDA pursuant to inspections that will be conducted after we submit an NDA to the FDA. We do not control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with the cGMP regulation for manufacture of both active drug substances and finished drug products. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities or our marketing applications will not be approved. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or a comparable foreign regulatory authority finds deficiencies with or does not approve these facilities for the manufacture of our product candidates or if it finds deficiencies or withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved. Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or voluntary recalls of product candidates or medicines, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our medicines and harm our business and results of operations.

Any products that we may develop may compete with our other product candidates and products and the products of third parties for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for a redundant supply of bulk drug substances. If any one of our current contract manufacturers cannot perform as agreed, we may be required to replace that manufacturer. Although we believe that there are several potential alternative manufacturers who could manufacture our product candidates, we may incur added costs and delays in identifying and qualifying any such replacement.

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

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain patent protection for our medicines and technology, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize medicines and technology similar or identical to ours, and our ability to successfully commercialize our medicines and technology may be adversely affected.

Our commercial success will depend, in part, on our ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary products and technology. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies and medicines that are important to our business, by pursuing the grant of patents from those applications around the world, and by taking steps to defend those patents if challenged by third parties. It is not uncommon in the pharmaceutical industry for patents covering successful drugs to be challenged for invalidity by third parties before or after the grant of such patents by a patent office (e.g., by a pre- or post-grant proceeding in a patent office or a court action). Currently we own five issued U.S. patents, several foreign patents and multiple pending applications worldwide that relate to our proprietary technology or product candidates. We cannot be certain that we will secure any additional rights to any issued patents with claims that cover any of our proprietary technology or product candidates.

The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection on or due to the public disclosures of others or ourselves. Although we enter into non-disclosure and confidentiality agreements with parties who have access to patentable aspects of our research and development output, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors and other third parties, any of these parties may breach the agreements and disclose such output before a patent application is filed, thereby jeopardizing our ability to seek patent protection.

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

In addition to seeking patents for some of our technology and medicines, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. With respect to our proprietary scientific insights, screening assays and manufacturing processes, we consider trade secrets and know-how to be our primary intellectual property. Trade secrets and know-how can be difficult to protect. In particular, we anticipate that with respect to our precision medicine platform, these trade secrets and know-how will over time be acquired within the industry through independent development, the publication of journal articles describing methodologies and insights, and the movement of personnel skilled in the art into the pharmaceutical and biotechnology industry.

We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets, and discovery processes to aid in proving trade secret misappropriation may be limited in many foreign countries. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third party, we may have no right to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third party, our competitive position could be harmed.

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

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including court actions for patent infringement or nullification, pre- and post-grant proceedings before the U.S. Patent and Trademark Office (USPTO), and corresponding proceedings in foreign patent offices. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are pursuing development candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our product candidates, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block or delay our ability to commercialize such product candidate unless we obtained a license under the applicable patents, or until such patents expire.

Parties making claims against us may also obtain injunctive or other equitable relief, which could effectively block or delay our ability to further develop and commercialize one or more of our product candidates. Defense of these claims, regardless of their merit, could involve substantial litigation expense and could be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may be required to take a number of steps, including but not limited to, paying substantial damages, including treble damages and attorneys' fees for willful infringement, paying lost profits or royalties, redesigning our infringing products or manufacturing process, obtaining one or more licenses from third parties for activities going forward, which may be impossible or require substantial time and monetary expenditure.

Parties making claims against us may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have material adverse effect on our ability to raise additional funds or otherwise have a material adverse effect on our business, results of operations, financial condition and prospects.

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

Competitors may infringe our patents or the patents of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid, is unenforceable and/or is not infringed, or may refuse to stop the other party from using the technology at issue for many reasons, including but not limited to, a determination that our patents do not cover the technology in question. Interference proceedings provoked by third parties or brought by us may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors or collaborators. An adverse result in any litigation or patent office proceeding could put one or more of our patents at risk, for example, of being invalidated, deemed unenforceable or interpreted narrowly or could put our patent applications at risk of not issuing.

An unfavorable outcome could require us to cease using a technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of our patents and patent applications may fail and, even if successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States.

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

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

We may also be subject to claims that third parties, including but not limited to, former employees and collaborators, have an ownership interest in our patents or other intellectual property. In the future, we may have ownership disputes arising, for example, from conflicting obligations of consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as the exclusive ownership of, or the right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation or arbitration could result in substantial costs and be a distraction to management and other employees.

Issued patents covering our product candidates could be found invalid or unenforceable if challenged in court.

If we or one of our licensing partners initiated legal proceedings against a third party to enforce a patent covering one of our product candidates or the use or manufacture thereof, the defendant could counterclaim that the patent covering our product candidate is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including utility, written description, novelty, non-obviousness or enablement. Additionally, in the United States, a patent can be deemed unenforceable if someone connected with the prosecution of a patent application intentionally withheld materially relevant information from the USPTO, or intentionally mislead the USPTO during prosecution. Third-party challenges to the validity and/or enforceability of a patent can occur in courts in the United States or abroad, or in pre- or post-grant proceedings in some foreign patent offices (e.g., but not limited to re-examination, post grant review, inter parties review, or opposition proceedings). Such proceedings could result in the revocation of, or amendment to, our patents in such a way that they no longer cover our product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability of one of our patents for a product candidate, this could substantially affect our ability to protect that product candidate in the country in which the patent was issued. Such a loss of patent protection could have a material adverse impact on our business.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties or that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.

As is common in the biotechnology and pharmaceutical industry, we employ individuals who were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and independent contractors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of any of our employee's former employer or other third parties. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages and suffering reputational harm, we may lose valuable intellectual property rights or personnel, which could adversely impact our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

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

Filing, prosecuting and defending patents on our product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and may also export infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with any products that we may develop and commercialize, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

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

Risks Related to Commercialization and the Market for Our Product Candidates

If the market opportunities for our product candidates are smaller than we believe they are or if we are unable to market our products to expanded patient populations, our revenues may be adversely affected, and our business may suffer.

We focus our research and product development efforts on treatments for cardiac muscle contraction and our targeted indications affect relatively small populations. In particular, we estimate that approximately 630,000 people in the United States have a form of HCM, and that approximately 360,000 people in the United States have a form of genetic DCM. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on estimates derived from primary research with physicians and payors, analysis of medical journals and peer-reviewed literature, the work of third-party consultants and other publicly- or non-publicly-available data sources. These estimates may prove to be incorrect and new studies may change the estimated incidence or prevalence of our targeted disease indications. The number of patients in the United States, Europe and elsewhere may turn out to be lower than expected, may not be otherwise amenable to treatment with our products, and new patients may become increasingly difficult to identify or gain access to, all of which would adversely affect our results of operations and our business.

Additionally, because the target patient populations of our product candidates are small, we must be able to successfully identify patients and achieve a significant market share to achieve or maintain profitability and growth.

Even if any of our product candidates receive marketing approval, they may fail to achieve the degree of market acceptance by physicians, patients, healthcare payors and others in the medical community necessary for commercial success.

If any of our product candidates receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, healthcare payors and others in the medical community. For example, current cardiovascular disease treatments such as beta blockers, non-dihydropyridine calcium channel blockers and disopyramide are well-established in the medical community, and doctors may continue to rely on these treatments. If our product candidates do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- efficacy and potential advantages compared to alternative treatments;
- the ability to offer our medicines for sale at competitive prices;
- convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- sufficient third-party coverage or reimbursement; and
- the prevalence and severity of any side effects.

Any failure to achieve or maintain sufficient market acceptance of mavacamten, danicamtiv or any of our other product candidates, if approved, could significantly harm our business, prospects, financial condition and results of operations.

If, in the future, we are unable to establish sales and marketing capabilities or enter into agreements with third parties to sell and market our drug candidates, we may not be successful in commercializing our drug candidates if and when they are approved, and we may not be able to generate any revenue.

We do not currently have a sales or marketing infrastructure and have limited experience in the sale, marketing or distribution of drugs. To achieve commercial success for any approved drug candidate for which we retain sales and marketing responsibilities, we must build our sales, marketing, managerial, and other non-technical capabilities or make arrangements with third parties to perform these services. In the future, we may choose to build a focused sales and marketing infrastructure to sell, or participate in sales activities with our collaborators for, some of our drug candidates if and when they are approved.

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

Factors that may inhibit our efforts to commercialize our drug candidates on our own include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future drugs;
- the lack of complementary drugs to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization

If we enter into arrangements with third parties to perform sales, marketing and distribution services, our drug revenues or the profitability of these drug revenues to us are likely to be lower than if we were to market and sell any drug candidates that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market our drug candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our drug candidates effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our drug candidates. Further, our business, results of operations, financial condition and prospects will be materially adversely affected.

The insurance coverage and reimbursement status of newly-approved products targeting small patient populations is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for our product candidates, if approved, could limit our ability to market those products and decrease our ability to generate revenue.

The availability and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford expensive treatments, such as endothelin receptor antagonists used in the treatment of certain cardiovascular diseases. Sales of our product candidates will depend substantially, both domestically and abroad, on the extent to which the costs of our product candidates will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third-party payors. Additionally, therapies directed at small patient populations, such as our product candidates, may be more expensive, and reimbursement options for these therapies may be more limited. If reimbursement or coverage is not available, or is available only to limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain pricing sufficient to realize a sufficient return on our investment.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products and for products whose targeted patient populations are small. In the United States, the principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services (CMS), an agency within the U.S. Department of Health and Human Services, as CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare. Private payors tend to follow CMS to a substantial degree. It is difficult to predict what CMS or third-party payors will decide with respect to reimbursement and coverage for fundamentally novel products such as ours, as there is no body of established practices and precedents for these new products. Reimbursement agencies in Europe may be more conservative than CMS.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe, Canada, and other countries may put pressure on the pricing and usage of our product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. In general, the prices of medicines under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for medicines but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenues and profits.

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

While we have received orphan drug designation for our most advanced drug candidate, mavacamten, for the treatment of symptomatic oHCM, we may seek orphan drug designation for some of our other drug candidates. However, we may be unsuccessful in obtaining or may be unable to maintain the benefits associated with orphan drug designation, including the potential for market exclusivity.

The FDA has granted orphan drug designation to mavacamten for the treatment of symptomatic oHCM. As part of our business strategy, we may seek orphan drug designation for some of our other drug candidates, and we may be unsuccessful. Regulatory authorities in some jurisdictions, including the United States, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug will be recovered from sales in the United States. In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers.

Generally, if a drug with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the drug is entitled to a period of marketing exclusivity, which precludes the FDA from approving another marketing application for the same drug and indication for that time period, except in limited circumstances. The applicable period is seven years in the United States. Even if we obtain orphan drug exclusivity for a drug, that exclusivity may not effectively protect the designated drug from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. In addition, a designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. Moreover, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition. Orphan drug designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process. While we might seek orphan drug designation for our other drug candidates in addition to mavacamten for the treatment of symptomatic oHCM, we may never receive such designations. Even if we receive orphan drug designation for any of our drug candidates, there is no guarantee that we will enjoy the benefits of those designations.

If we participate in and then fail to comply with our reporting and payment obligations under governmental pricing programs in the United States, we could be subject to additional reimbursement requirements, penalties, sanctions and fines which could have a material adverse effect on our business financial condition, results of operations and growth prospects.

With the approval of any product candidate, we anticipate that we may participate in a number of federal and state government pricing programs in the United States in order to obtain coverage for the product by certain government healthcare programs. These programs would generally require us to pay rebates or provide discounts to certain private purchasers or government payers in connection with our products when dispensed to beneficiaries of these programs. In some cases, such as with the Medicaid Drug Rebate Program, the rebates are based on pricing and rebate calculations that we report on a monthly and quarterly basis to the government agencies that administer the programs. The terms, scope and complexity of these government pricing programs change frequently. We may also have reimbursement obligations or be subject to penalties if we fail to provide timely and accurate information to the government, pay the correct rebates or offer the correct discounted pricing. Changes to the price reporting or rebate requirements of these programs would affect our obligations to pay rebates or offer discounts. Responding to current and future changes may increase our costs and the complexity of compliance, will be time-consuming, and could have a material adverse effect on our results of operations.

Risks Related to Our Business and Industry

We may be subject to healthcare, health information privacy and security laws, regulation and enforcement, and our failure to comply with these laws could harm our results of operations and financial conditions.

Although we do not currently have any products on the market, if we obtain FDA approval for any of our product candidates and begin commercializing those products in the United States, our operations may be directly, or indirectly through our customers and third-party payors, subject to various U.S. federal and state fraud and abuse, patient privacy and other healthcare regulatory laws, and to additional healthcare, statutory and regulatory requirements and enforcement by foreign regulatory authorities in jurisdictions in which we conduct our business. Healthcare providers, physicians and other healthcare market participants play a primary role in the recommendation and prescription of any product for which we obtain marketing approval. These laws may impact, among other things, our proposed sales, marketing and education programs and constrain the business of financial arrangements and relationships with healthcare providers, physicians and other parties through which we market, sell and distribute our products for which we obtain marketing approval. There are ambiguities as to what is required to comply with these requirements, and if we fail to comply with any applicable federal, state or foreign legal requirement, we could be subject to penalties.

Regulators globally are also imposing greater monetary fines for privacy violations. For example, in 2016, the European Union adopted a new regulation governing data practices and privacy called the General Data Protection Regulation (GDPR) which became effective on May 25, 2018. The GDPR applies to any company established in the European Union as well as to those outside the European Union if they collect and use personal data in connection with the offering goods or services to individuals in the European Union or the monitoring of their behavior. The GDPR enhances data protection obligations for processors and controllers of personal data, including, for example, special protections for “sensitive information” such as health and genetic information, expanded disclosures about how personal information is to be used, limitations on retention of information, mandatory data breach notification requirements and onerous new obligations on service providers. Non-compliance with the GDPR may result in monetary penalties of up to €20 million or 4% of worldwide revenue, whichever is higher. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of personal data, such as healthcare data or other sensitive information, could greatly increase our cost of developing or commercializing our product candidates or impair our ability to collect data from patients resident in the European Union, and we may be required to put in place additional mechanisms to ensure compliance with the GDPR, including as implemented by individual countries.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that may apply to us, we may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, exclusion from U.S. government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs and imprisonment. If any of the above occur, it could adversely affect our ability to operate our business and our results of operations.

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

Our competitors may develop drugs that are less expensive, safer, or more effective, which may diminish or eliminate the commercial success of any drugs that we may commercialize.

Our competitors may:

- develop drug candidates and market drugs that are less expensive or more effective than our future drugs;
- commercialize competing drugs before we or our partners, if any, can launch any drugs developed from our drug candidates;
- initiate or withstand substantial price competition more successfully than we can;
- have greater success in recruiting skilled scientific workers from the limited pool of available talent;
- more effectively negotiate third-party licenses and strategic collaborations; and
- take advantage of acquisition or other opportunities more readily than we can.

We will compete for market share against large pharmaceutical and biotechnology companies and smaller companies that are collaborating with larger pharmaceutical companies, new companies, academic institutions, government agencies and other public and private research organizations. Many of these competitors, either alone or together with their partners, may develop new drug candidates that will compete with ours, as these competitors may, and in certain cases do, operate larger research and development programs or have substantially greater financial resources than we do. Our competitors may also have significantly greater experience in:

- developing product candidates;
- undertaking preclinical testing and clinical trials;
- building relationships with key customers and opinion-leading physicians;
- obtaining and maintaining FDA and other regulatory approvals of product candidates;
- formulating and manufacturing drugs; and
- launching, marketing and selling drugs.

If our competitors market drugs that are less expensive, safer or more effective than our potential drugs, or that reach the market sooner than our potential drugs, we may not achieve commercial success. In addition, the life sciences industry is characterized by rapid technological change. Because our research approach integrates many technologies, it may be difficult for us to stay abreast of the rapid changes in each technology. If we fail to stay at the forefront of technological change, we may be unable to compete effectively. Our competitors may render our technologies obsolete by advances in existing technological approaches or the development of new or different approaches, potentially eliminating the advantages in our drug discovery process that we believe we derive from our research approach and proprietary technologies.

In the field of heart failure drug development, our principal competitors include Amgen Inc., AstraZeneca plc, Bayer AG, Bristol-Myers Squibb Company, C.H. Boehringer Sohn AG & Co. KG, Eli Lilly and Company, Novartis AG and Takeda Pharmaceutical Company Limited. Specific to our initial drug discovery and development focus areas, we believe that Cytokinetics, Inc., Takeda Pharmaceutical Company Limited and Novartis AG have ongoing programs in HCM and that Novartis AG, Pfizer Inc., Tenaya Therapeutics, Berlin Cures, and Zensun (Shanghai) Sci. & Tech. Co., Ltd. have ongoing programs in DCM. Additionally, there may be other companies pursuing therapeutic candidates from which we face current or future competition.

Public opinion and heightened regulatory scrutiny of precision medicine for the treatment of cardiovascular disease may impact public perception of our product candidates or adversely affect our ability to conduct our business or obtain regulatory approvals for our product candidates.

Precision medicine remains a novel technology, particularly in the field of cardiovascular disease, with no products approved to date in the United States that are specifically targeted at correcting the underlying biomechanical defects in cardiac contractility associated with HCM and DCM. Public perception may be influenced by claims that these therapies are unproven or unsafe, and our product candidates may not gain the acceptance of the public or the medical community. In particular, our success will depend upon physicians, who specialize in the treatment of those diseases that our product candidates target, prescribing treatments that involve the use of our product candidates in lieu of, or in addition to, existing treatments they are already familiar with and for which greater clinical data may be available. More restrictive government regulations or negative public opinion could have an adverse effect on our business or financial condition and may delay or impair the development and commercialization of our product candidates or demand for any products we may develop. Adverse events in our clinical trials, even if not ultimately attributable to our product candidates, and the resulting publicity, could result in increased governmental regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates.

Healthcare legislative changes may have a material adverse effect on our business and results of operations.

In the United States, the European Union and other foreign jurisdictions, there have been a number of legislative and regulatory changes to the healthcare system that could affect our future results of operations. In particular, there have been and continue to be a number of initiatives at the United States federal and state levels that seek to reduce healthcare costs and improve the quality of healthcare. For example, the Patient Protection and Affordable Care Act (ACA) changed the way healthcare is financed by both governmental and private insurers and significantly impacted the U.S. pharmaceutical and biotechnology industries. Since its enactment, there have been many judicial, Presidential, and Congressional challenges to numerous aspects of the ACA, and the long ranging effects of these challenges on reimbursement by third-party payors, the viability of the ACA marketplace, providers, and potentially, our business are unknown at this time. In addition, the full impact of the ACA, any law repealing and/or replacing elements of it, and the political uncertainty surrounding any repeal or replacement legislation on our business remains unclear.

Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, CMS may develop new payment and delivery models, such as bundled payment models. The U.S. federal government has set a goal of moving 50% of Medicare payments into these “Alternative Payment Models” by the end of 2018. In addition, recently there has been heightened governmental scrutiny over the manner in which drug manufacturers set prices for their commercial products. We expect that additional U.S. federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U.S. federal government will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

In addition, other legislative changes have been proposed and adopted in the United States since ACA was enacted. On August 2, 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation’s automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of 2% per fiscal year. These reductions went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2025 unless additional Congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other health care funding, which could have a material adverse effect on our customers and accordingly, our financial operations.

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

We are highly dependent on our scientific advisors and the principal members of our executive team, the loss of whose services may adversely impact the achievement of our objectives. While we have entered into employment agreements with each of our executive officers, any of them could leave our employment at any time, as all of our employees are “at will” employees. Recruiting and retaining other qualified employees, consultants and advisors for our business, including scientific and technical personnel, will also be critical to our success. There is currently a shortage of skilled executives and scientific experts in our industry, which is likely to continue. As a result, competition for skilled personnel is intense and the turnover rate can be high. We may not be able to attract and retain personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies, as well as from academic and research institutions, for individuals with similar skill sets. In addition, any failure of our programs to succeed in preclinical studies or clinical trials may make it more challenging to recruit and retain qualified personnel. The inability to recruit or the loss of the services of any executive, key employee, consultant or advisor may impede the progress of our research, development and commercialization objectives.

We will need to expand our organization and we may experience difficulties in managing this growth, which could disrupt our operations.

As of December 31, 2019, we had 235 full-time employees. As we mature, we expect to expand our full-time employee base and to hire more consultants and contractors. Over the next several years, we expect to expand our development, regulatory and sales and marketing capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations. Our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and/or grow revenues could be reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth.

We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on research programs and product candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial medicines or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable medicines. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

Inadequate funding for the FDA, the SEC and other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, including most recently from December 22, 2018 to January 25, 2019, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Our anticipated international operations may expose us to business, regulatory, political, operational, financial, pricing and reimbursement and economic risks associated with doing business outside of the United States.

We have two wholly-owned subsidiaries: an Australian subsidiary through which we conduct clinical trials in Australia and a Dutch subsidiary through which we intend to determine the feasibility of commercialization in the EU. Our business strategy also contemplates potential additional international operations as we seek to continue the development of mavacamten, danicamtiv, MYK-224 and other product candidates that we have or may identify, seek regulatory approval for our product candidates, and commercialize any product candidates that are approved outside the United States. If any product candidates for which we have retained worldwide commercial rights are approved, we may hire sales representatives and conduct physician and patient group outreach activities outside of the United States. Doing business internationally involves a number of risks, including but not limited to:

- multiple, conflicting, and changing laws and regulations such as privacy regulations, tax laws, export and import restrictions, employment laws, regulatory requirements, and other governmental approvals, permits, and licenses;
- failure by us to obtain and maintain regulatory approvals for the use of our products in various countries;
- complexities and difficulties in obtaining protection for and enforcing our intellectual property rights;
- difficulties in staffing and managing foreign operations;

- complexities associated with managing multiple payor reimbursement regimes, government payors, or patient self-pay systems;
- limits in our ability to penetrate international markets;
- financial risks, such as exposure to foreign currency exchange rate fluctuations and their impact on payments required in local currency;
- natural disasters, political and economic instability, including wars, terrorism, and political unrest, outbreak of disease, boycotts, curtailment of trade, and other business restrictions (such as the outbreak of the novel strain of coronavirus in December 2019);
- certain expenses including, among others, expenses for travel, translation, and insurance; and
- regulatory and compliance risks that relate to maintaining accurate information and control over sales and activities that may fall within the purview of the U.S. Foreign Corrupt Practices Act, its books and records provisions, or its anti-bribery provisions.

Any of these factors could significantly harm our future international expansion and operations and, consequently, our results of operations.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials or other work-related injuries, this insurance may not provide adequate coverage against potential liabilities. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Our employees, independent contractors, principal investigators, CROs, consultants, vendors and collaboration partners may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have a material adverse effect on our business.

We are exposed to the risk that our employees, independent contractors, principal investigators, CROs, consultants, vendors and collaboration partners may engage in fraudulent conduct or other illegal activities. Misconduct by these parties could include intentional, reckless and/or negligent conduct or unauthorized activities that violate: (i) the regulations of the FDA, EMA and other regulatory authorities, including those laws that require the reporting of true, complete and accurate information to such authorities; (ii) manufacturing standards; (iii) federal and state data privacy, security, fraud and abuse and other healthcare laws and regulations in the United States and abroad; or (iv) laws that require the reporting of true, complete and accurate financial information and data. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Activities subject to these laws could also involve the improper use of information obtained in the course of clinical trials or creating fraudulent data in our preclinical studies or clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent misconduct may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with such laws or regulations. Additionally, we are subject to the risk that a person could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other U.S. federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Unfavorable global economic and political conditions could adversely affect our business, financial condition or results of operations.

Our ability to invest in and expand our business and meet our financial obligations, to attract and retain third-party contractors and collaboration partners and to raise additional capital depends on our operating and financial performance, which, in turn, is subject to numerous factors, including the prevailing economic and political conditions and financial, business and other factors beyond our control, such as the rate of unemployment, the number of uninsured persons in the United States, political influences and inflationary pressures. For example, an overall decrease in or loss of insurance coverage among individuals in the United States as a result of unemployment, underemployment or the potential repeal of certain provisions of the ACA, may decrease the demand for healthcare services and pharmaceuticals. If fewer patients are seeking medical care because they do not have insurance coverage, we may experience difficulties in any eventual commercialization of our product candidates and our business, results of operations, financial condition and cash flows could be adversely affected.

In addition, our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets upon which biopharmaceutical companies such as us are dependent for sources of capital. In the past, global financial crises have caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn could result in a variety of risks to our business, including a reduced ability to raise additional capital when needed on acceptable terms, if at all, and weakened demand for our product candidates. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

We or the third parties upon whom we depend may be adversely affected by earthquakes, outbreak of disease or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Our corporate headquarters is located in the San Francisco Bay Area, which in the past has experienced severe earthquakes. Earthquakes, outbreak of disease, or other natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as the manufacturing facilities of our third-party contract manufacturers, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. For example, in December 2019, an outbreak of a novel strain of coronavirus originated in Wuhan, China. Since the manufacturing facilities of some of our third-party contract manufacturers are in China, an outbreak of communicable diseases in China or elsewhere, or the perception that such an outbreak could occur, and the measures taken by the governments of countries affected, could adversely affect our business, financial condition or results of operations by limiting our ability to obtain supplies of product candidates for our clinical trials from manufacturers within or outside China and force temporary closure of facilities that we rely upon. The extent to which the coronavirus impacts our results will depend on future developments, which are highly uncertain and cannot be accurately predicted, including new information which may emerge concerning the severity of the coronavirus and the actions to contain the coronavirus or treat its impact, among others. The disaster recovery and business continuity plans we have in place currently are limited and are unlikely to prove adequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business.

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

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

- decreased demand for any product candidates or medicines that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and
- the inability to commercialize mavacamten, danicamtiv, MYK-224 or any other product candidates that we may develop.

Although we maintain product liability insurance, including coverage for clinical trials that we sponsor, it may not be adequate to cover all liabilities that we may incur. We anticipate that we will need to increase our insurance coverage as we commence additional clinical trials and if we successfully commercialize any product candidates. The market for insurance coverage is increasingly expensive, and the costs of insurance coverage will increase as our clinical programs increase in size. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

Our internal computer systems, or those of our third-party CROs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our operations.

Despite the implementation of security measures, our internal computer systems and those of our third-party CROs and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our programs. For example, the loss of clinical trial data for our product candidates could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications or other data or applications relating to our technology or product candidates, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and experience delays or disruptions to various aspects of our operations, including our financial reporting and the development of our product candidates.

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

We have incurred substantial losses during our history and do not expect to become profitable in the near future. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any, until such unused losses expire. Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (the Code) if a corporation undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership over a rolling three-year period, the corporation's ability to use its pre-change net operating loss carryforwards (NOLs) and other pre-change tax attributes (such as research tax credits) to offset its post-change income or taxes may be limited. While we have determined that an ownership change occurred in April 2015 in connection with our Series B redeemable convertible preferred stock financing and in August 14, 2017 due to a subsequent stock offering, we do not believe that these ownership changes will result in the expiration of any of our existing NOLs prior to utilization. We may experience subsequent shifts in our stock ownership, some of which are outside our control. As a result, if we earn net taxable income, our ability to use our pre-change net operating loss carryforwards to offset U.S. federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

In addition, under the Tax Act, the amount of post-2017 NOLs that we are permitted to deduct in any taxable year is limited to 80% of our taxable income in such year, where taxable income is determined without regard to the NOL deduction itself. The Tax Act generally eliminates the ability to carry back any NOL to prior taxable years, while allowing post-2017 unused NOLs to be carried forward indefinitely. There is a risk that due to changes under the Tax Act, regulatory changes or other unforeseen reasons, our existing NOLs could expire or otherwise be unavailable to offset future income tax liabilities.

The United Kingdom's withdrawal from the EU may have a negative effect on our business, global economic conditions, and financial markets.

As a result of the United Kingdom's vote to leave the EU in March 2019 (known as Brexit), the EMA relocated its headquarters from London to Amsterdam. Since a significant proportion of the regulatory framework in the United Kingdom is derived from EU directives and regulations, Brexit could materially impact the regulatory regime with respect to the approval of product candidates, disrupt the manufacture of our products and product candidates in the United Kingdom or the EU, disrupt the import and export of active substances and other components of drug formulations, and disrupt the supply chain for clinical trial product and final authorized formulations. While negotiations continue regarding the terms of the United Kingdom's withdrawal from the EU, the specific impact to the supervision, regulation and supply of medicines in the United Kingdom and Europe remain unclear. The cumulative effect of disruptions to the regulatory framework or supply chains may add considerably to the development lead time to, and expense of, marketing authorization and commercialization of products in the EU and/or the United Kingdom. In view of the uncertainty surrounding the Brexit implementation, we are unable to predict the effects of such disruption to the regulatory framework and supply chain in Europe.

Risks Related to Our Common Stock

The market price of our common stock has been and may continue to be highly volatile.

The market price of our common stock has experienced volatility since our IPO in October 2015 and is likely to continue to be volatile. Our stock price could be subject to wide fluctuations in response to a variety of factors, including the following:

- adverse results or delays in preclinical studies or clinical trials;
- failure to develop successfully and commercialize our product candidates;
- inability to obtain additional funding;
- any delay in filing an IND or NDA for any of our product candidates and any adverse development or perceived adverse development with respect to the FDA's review of that IND or NDA;
- failure by us or our licensors and strategic collaborators, if any, to prosecute, maintain or enforce our intellectual property rights;
- changes in laws or regulations applicable to future products;
- inability to obtain adequate product supply for our product candidates or the inability to do so at acceptable prices;
- adverse regulatory decisions affecting our product candidates or development programs;
- introduction of new products, services or technologies by our competitors;
- failure to meet or exceed financial projections we may provide to the public or to the investment community;
- the perception of the pharmaceutical industry by the public, legislatures, regulators and the investment community;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us, our strategic collaboration partner or our competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- additions or departures of key scientific or management personnel;
- significant lawsuits, including patent or stockholder litigation;
- changes in the market valuations of similar companies;
- sales of our common stock by us or our stockholders in the future; and
- trading volume of our common stock.

In addition, companies trading in the stock market in general, and the NASDAQ Global Select Market (NASDAQ) in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. In the past, following periods of volatility in the market, securities class-action litigation has often been instituted against companies. Such litigation, if instituted against us, could result in substantial costs and diversion of management's attention and resources, which could materially and adversely affect our business, financial condition, results of operations and growth prospects.

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

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

In addition, sales of a substantial number of shares of our outstanding common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock. A substantial number of our outstanding shares of common stock are held by a relatively small number of stockholders who are not subject to restrictions on trading. Sales by our stockholders of a substantial number of shares, or the expectation that such sales may occur, could significantly reduce the market price of our common stock.

We have also registered all shares of our common stock subject to options or other equity awards issued or reserved for future issuance under our equity incentive plans. As a result, these shares will be eligible for sale in the public market to the extent permitted by any applicable vesting requirements and the exercise of options, and restrictions under applicable securities laws. In addition, our directors, executive officers and certain affiliates have established or may in the future establish programmed selling plans under Rule 10b5-1 of the Securities Exchange Act of 1934, as amended, for the purpose of effecting sales of our common stock. If any of these events cause a large number of our shares to be sold in the public market, the sales could reduce the trading price of our common stock and impede our ability to raise future capital. If these additional shares are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

Pursuant to our 2015 Stock Option and Incentive Plan (the 2015 Plan), we are authorized to grant stock options and other equity-based awards to our employees, directors and consultants. Beginning on January 1, 2017, the number of shares available for future grant under the 2015 Plan will automatically increase each year by up to 4% of all shares of our capital stock outstanding as of December 31 of the prior calendar year, subject to the ability of our board of directors to take action to reduce the size of the increase in any given year. In addition, beginning on January 1, 2017 and ending on January 1, 2025, the number of shares available for future issuance under our 2015 Employee Stock Purchase Plan (the 2015 ESPP) will automatically increase each year by up to the lesser of 3,000,000 shares of common stock or 1% of all shares of our capital stock outstanding as of December 31 of the prior calendar year, subject to the ability of our board of directors to take action to reduce the size of the increase in any given year. Currently, we plan to register the increased number of shares available for issuance under the 2015 Plan and the 2015 ESPP each year. If our board of directors elects to increase the number of shares available for future grant under these plans by the maximum amount each year, our stockholders may experience additional dilution, which could cause our stock price to fall.

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

As of February 14, 2020, our executive officers, directors, 5% or greater stockholders and their affiliates beneficially own approximately 50.7% of our outstanding voting stock. These stockholders will have the ability to influence us through their ownership positions. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders, acting together, may be able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may believe are in your best interest as one of our stockholders.

We have broad discretion in the use of our cash and cash equivalents and may not use them effectively.

Our management has broad discretion in the application of our existing cash and cash equivalents, and you will not have the opportunity to assess whether our existing cash and cash equivalents are being used appropriately. Because of the number and variability of factors that will determine our use of our existing cash and cash equivalents, their ultimate use may vary substantially from their currently intended use. The failure by our management to apply these funds effectively could harm our business. Pending their use, we may invest our cash and cash equivalents in short-term, investment-grade, interest-bearing securities. These investments may not yield a favorable return to our stockholders.

If securities or industry analysts do not publish research, or publish inaccurate or unfavorable research, about our business, our stock price and trading volume could decline.

The trading market for our common stock will depend, in part, on the research and reports that securities or industry analysts publish about us or our business. Securities and industry analysts may not publish an adequate amount of research on our company, which may negatively impact the trading price for our stock. In addition, if one or more of the analysts who cover us downgrade our stock or publish inaccurate or unfavorable research about our business, our stock price would likely decline. Further, if our operating results fail to meet the forecasts of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

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

As a public company, we incur and will continue to incur significant legal, accounting and other expenses. In addition, the Sarbanes-Oxley Act and rules subsequently implemented by the SEC and NASDAQ have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel have devoted and will continue to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased and will continue to increase our legal and financial compliance costs and will make some activities more time-consuming and costly.

Pursuant to Section 404 of the Sarbanes-Oxley Act, we are required to furnish a report by our management on our internal control over financial reporting with our Annual Report on Form 10-K for each fiscal year and to obtain an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we are and will continue to be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, engage outside consultants and adhere to a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting.

Despite our efforts, there is a risk that neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. This could impair our ability to produce timely and accurate consolidated financial statements and result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our consolidated financial statements.

In addition, as a public company we are required to file accurate and timely quarterly, annual and current reports with the SEC under the Exchange Act. Any failure to report our financial results on an accurate and timely basis could result in sanctions, lawsuits, delisting of our shares from The Nasdaq Global Select Market or other adverse consequences that would materially harm our business.

Our operating results may fluctuate significantly or may fall below the expectations of investors or securities analysts, each of which may cause our stock price to fluctuate or decline.

Our quarterly and annual operating results may fluctuate significantly in the future, which makes it difficult to predict our future operating results. Our net loss and other operating results will be affected by numerous factors, many of which are outside of our control and may be difficult to predict, including:

- variations in the level of expenses related to our clinical development programs, our precision medicine platform or our preclinical research and development programs;
- the timing and success or failure of preclinical studies and clinical trials for our product candidates or competing product candidates;
- our ability to obtain regulatory approval for our product candidates, and the timing and scope of any such approvals we may receive;
- if any of our product candidates receives regulatory approval, the level of underlying demand for these product candidates and our ability to successfully commercialize any approved product;
- addition or termination of clinical trials or funding support;
- our execution of any new collaborative, licensing or similar arrangements, and the timing of payments we may make or receive under these arrangements;
- any intellectual property infringement or other lawsuits in which we may become involved; and
- regulatory developments affecting our product candidates or those of our competitors.

If our operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially. Additionally, due to the unpredictability of our quarterly and annual operating results, we believe that period-to-period comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of our future performance.

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

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

We could be subject to securities class action litigation.

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

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us or increase the cost of acquiring us, even if doing so would benefit our stockholders or remove our current management.

Our amended and restated certificate of incorporation, amended and restated bylaws and Delaware law contain provisions that may have the effect of delaying or preventing a change in control of us or changes in our management. Our amended and restated certificate of incorporation and amended and restated bylaws include provisions that:

- authorize "blank check" preferred stock, which could be issued by our board of directors without stockholder approval and may contain voting, liquidation, dividend and other rights superior to our common stock;
- create a classified board of directors whose members serve staggered three-year terms;
- specify that special meetings of our stockholders can be called only by our board of directors, the chairperson of our board of directors, our chief executive officer or our president;
- prohibit stockholder action by written consent;
- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;
- provide that our directors may be removed only for cause and with the vote of the holders of 75% or more of our outstanding capital stock then entitled to vote at an election of directors;
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even if less than a quorum;
- specify that no stockholder is permitted to cumulate votes at any election of directors;
- expressly authorize our board of directors to modify, alter or repeal our amended and restated bylaws; and
- require supermajority votes of the holders of our common stock to amend specified provisions of our amended and restated certificate of incorporation and amended and restated bylaws.

These provisions, alone or together, could delay or prevent hostile takeovers and changes in control or changes in our management.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15% of our outstanding voting stock to merge or combine with us.

Any provision of our amended and restated certificate of incorporation or amended and restated bylaws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock and could also affect the price that some investors are willing to pay for our common stock.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

For a description of our properties, please see Note 6 "Leases" of the Notes to Consolidated Financial Statements included in Item 8 of this Annual Report on Form 10-K, which is incorporated herein by reference.

ITEM 3. LEGAL PROCEEDINGS

We are not a party to any material legal proceedings. From time to time, we may be subject to various legal proceedings and claims that arise in the ordinary course of our business activities. Although the results of litigation and claims cannot be predicted with certainty, we do not believe we are party to any claim or litigation the outcome of which, if determined adversely to us, would individually or in the aggregate be reasonably expected to have a material adverse effect on our business. Regardless of the outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

ITEM 4. MINE SAFETY DISCLOSURES

None.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

MARKET INFORMATION

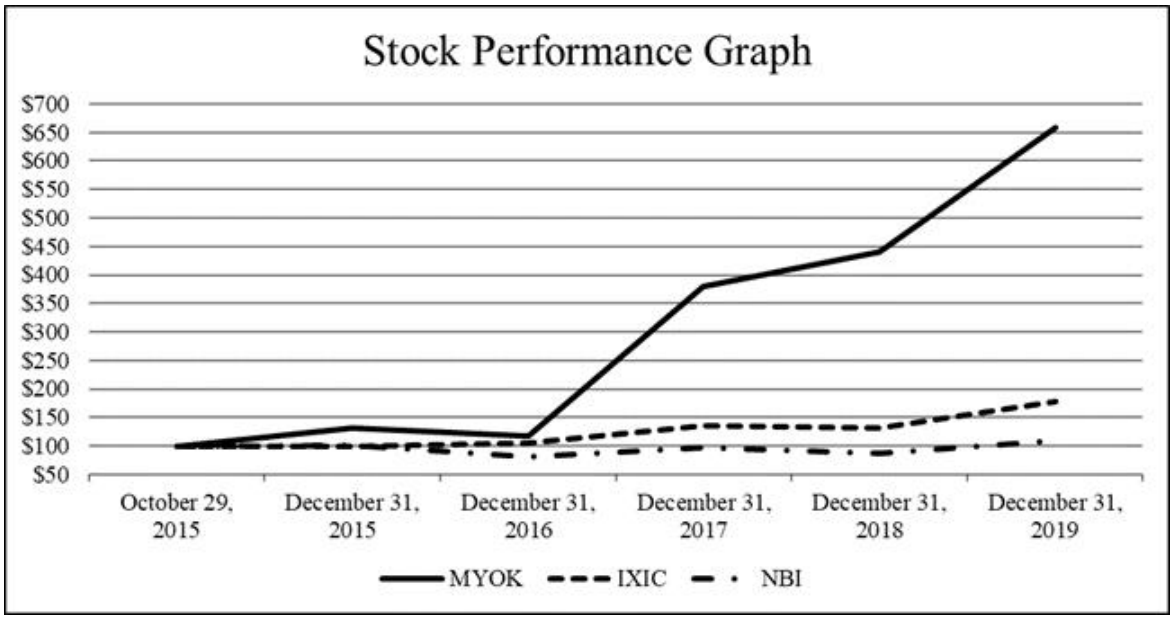
Our common stock began trading on The NASDAQ Global Select Market under the symbol "MYOK" on October 29, 2015. Prior to this date, there was no public market for our common stock.

HOLDERS OF COMMON STOCK

As of February 24, 2020, we had 46,574,538 shares of common stock outstanding held by approximately 6 stockholders of record. We believe that the number of beneficial owners of our common stock at that date was substantially greater. The approximate number of holders is based upon the actual number of holders registered in our records at such date and excludes holders in "street name" or persons, partnerships, associations, corporations, or other entities identified in security positions listings maintained by depository trust companies.

STOCK PERFORMANCE GRAPH

The following graph illustrates a comparison of the total cumulative stockholder return on our common stock since October 29, 2015, which is the date our common stock first began trading on the NASDAQ Global Select Market, to two indices: the NASDAQ Composite Index and the NASDAQ Biotechnology Index. The stockholder return shown in the graph below is not necessarily indicative of future performance, and we do not make or endorse any predictions as to future stockholder returns. This graph shall not be deemed "soliciting material" or be deemed "filed" for purposes of Section 18 of the Exchange Act, or otherwise subject to the liabilities under that Section, and shall not be deemed to be incorporated by reference into any of our filings under the Securities Act, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.



Assumed $100 investment in stock or index	Ticker	October 29, 2015	December 31, 2015	December 31, 2016	December 31, 2017	December 31, 2018	December 31, 2019
MyoKardia, Inc. (MYOK)	MYOK	$ 100	$ 132	$ 117	$ 380	$ 441	$ 658
NASDAQ Composite (^IXIC)	IXIC	$ 100	$ 99	$ 106	$ 136	$ 131	$ 177
NASDAQ Biotechnology (^NBI)	NBI	$ 100	$ 102	$ 80	$ 97	$ 88	$ 109

DIVIDEND POLICY

We have never declared or paid cash dividends on our capital stock. We currently expect to retain all future earnings, if any, for use in the operation and expansion of our business, and therefore do not anticipate paying any cash dividends in the foreseeable future.

SECURITIES AUTHORIZED FOR ISSUANCE UNDER EQUITY COMPENSATION PLANS

Information about our equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report on Form 10-K.

RECENT SALES OF UNREGISTERED SECURITIES

None.

ISSUER PURCHASES OF EQUITY SECURITIES

Period	(a) Total Number of Shares Purchased	(b) Average Price Paid per Share	(c) Total Number of Shares Purchased as Part of Publicly Announced Plans or Programs	(d) Maximum Number (or Approximate Dollar Value) of Shares that May Yet Be Purchased Under the Plans or Programs
		(in thousands, except per share amounts)		
October 1, 2019 through October 31, 2019	—	$ —	—	—
November 1, 2019 through November 30, 2019	—	—	—	—
December 1, 2019 through December 31, 2019	—	—	—	—
Total	—	$ —	—	—

ITEM 6. SELECTED CONSOLIDATED FINANCIAL DATA

You should read the selected historical financial data below in conjunction with the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and the consolidated financial statements and related notes included elsewhere in this Annual Report on Form 10-K. The selected financial data set forth below may not be indicative of future operating results.

	Year Ended December 31,				
(In thousands, except per share data)	2019	2018	2017 (1)	2016 (1)	2015
Consolidated Statement of Operations Data:					
Collaboration and license revenue	$ —	$ 33,558	$ 11,442	$ 41,971	$ 14,199
Operating expenses:					
Repurchase of royalty rights	80,000	—	—	—	—
Research and development	146,171	68,774	48,136	36,215	28,393
Selling, general and administrative	61,663	38,435	21,973	16,289	9,019
Total operating expenses	287,834	107,209	70,109	52,504	37,412
Loss from operations	(287,834)	(73,651)	(58,667)	(10,533)	(23,213)
Interest and other income (loss), net	11,621	5,953	1,657	153	(47)
Change in fair value of redeemable convertible preferred stock call option liability	—	—	—	—	314
Net loss	$ (276,213)	$ (67,698)	$ (57,010)	$ (10,380)	$ (22,946)
Net loss per share, basic and diluted	$ (6.17)	$ (1.76)	$ (1.74)	$ (0.38)	$ (4.48)

(1) The Company revised the consolidated statements of operations for the years ended December 31, 2017 and 2016 to reflect the adoption of ASC 606 "Revenue from Contracts with Customers" effective January 1, 2016. The consolidated statement of operation data for the year ended December 31, 2015 has not been revised.

(In thousands)	As of December 31, 2019	2018	2017 (1)	2016 (1)	2015
Consolidated Balance Sheet Data:					
Cash and cash equivalents	$ 101,436	$ 246,122	$ 224,571	$ 135,797	$ 112,265
Working capital	$ 375,924	$ 282,769	$ 207,463	$ 164,333	$ 91,572
Total assets	$ 456,094	$ 407,253	$ 282,808	$ 201,306	$ 116,580
Accumulated deficit	$ (478,766)	$ (202,553)	$ (134,855)	$ (77,837)	$ (64,685)
Total stockholders' equity	$ 406,274	$ 370,567	$ 230,676	$ 145,382	$ 93,873

(1) The Company revised certain consolidated balance sheet data as of December 31, 2017 and 2016 to reflect the adoption of ASC 606 "Revenue from Contracts with Customers" effective January 1, 2016. The consolidated balance sheet data as of December 31, 2015 has not been revised.

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

You should read the following discussion and analysis together with "Item 6. Selected Consolidated Financial Data" and our financial statements and related notes included elsewhere in this Annual Report. The following discussion contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those expressed or implied in any forward-looking statements as a result of various factors, including those set forth under the caption "Item 1A. Risk Factors."

Overview

We are a clinical-stage biopharmaceutical company pioneering a precision medicine approach to discover, develop and commercialize targeted therapies for the treatment of serious cardiovascular diseases. Our goal is to be the world's leading precision cardiovascular medicine company. Precision medicine involves discovering and developing therapies that integrate clinical and molecular information based on the biological basis of disease. Our strategy is to identify homogenous subgroups of patients with a given cardiovascular disease, understand the causal factors underlying that subgroup's condition, and develop targeted therapies designed to correct the common underlying defect leading to abnormal cardiac contraction or relaxation within each subgroup.

Our lead clinical-stage candidate is mavacamten, a novel, oral, allosteric modulator of cardiac myosin being developed for the treatment of hypertrophic cardiomyopathy (HCM). Mavacamten is intended to reduce cardiac muscle contractility by inhibiting the excessive myosin-actin cross-bridge formation that underlies the excessive contractility, left ventricular hypertrophy and reduced compliance characteristic of HCM. In 2016, mavacamten was granted Orphan Drug Designation by the United States Food and Drug Administration (FDA) for the treatment of symptomatic obstructive HCM. We are currently conducting a Phase 3 pivotal study of mavacamten, known as EXPLORER-HCM mavacamten in patients with symptomatic obstructive (New York Heart Association or NYHA Class II or III) HCM. Enrollment in the EXPLORER study completed in August 2019 at clinical sites in the United States, Europe, and Israel. Topline data from the EXPLORER-HCM trial are anticipated in the second quarter of 2020. Pending the outcome of this study, we plan to file a New Drug Application seeking regulatory approval of mavacamten for the treatment of obstructive HCM.

In addition to the EXPLORER-HCM study of mavacamten, the MAVA long-term extension (LTE) study of mavacamten is enrolling patients who have completed our Phase 3 EXPLORER-HCM trial or the Phase 2 MAVERICK-HCM in non-obstructive patients.

MAVERICK-HCM is a Phase 2 clinical study initiated in 2018 for the potential treatment of symptomatic non-obstructive HCM. In November 2019, we reported positive top-line results and established safety and tolerability of mavacamten in non-obstructive HCM over a treatment period of 16 weeks. Meaningful reductions in biomarkers of cardiac stress were observed in patients receiving mavacamten versus those in the placebo cohort and clear signals of clinical benefit were noted in a subgroup with elevated cardiac filling pressures and in a pre-specified group of patients at higher risk for morbidity and mortality. Based on the safety and pharmacologic benefits observed in the MAVERICK-HCM study, we plan to advance mavacamten into additional studies in defined groups of patients with non-obstructive HCM and heart failure with preserved ejection fraction (HFpEF).

In mid-2020, we plan to begin patient enrollment in the VALOR-HCM study to evaluate mavacamten as a therapeutic alternative to septal reduction therapy (SRT) in obstructive HCM patients. SRT is a highly invasive procedure consisting of a surgical or catheter-based therapy that eliminates or reduces the left ventricular outflow tract obstruction.

We are also conducting PIONEER-OLE, an open label extension study of obstructive HCM patients from our Phase 2 PIONEER trial. Data for twelve patients at 48 weeks of treatment with mavacamten were consistent with prior safety and efficacy observations at the 12, 24, and 36-week readouts. Highlights of the data included continued safety and tolerability and sustained clinical benefits, including reductions in left ventricular outflow tract (LVOT) gradient, improvements in New York Heart Association functional class and improvement of multiple biomarkers toward normal ranges. A reduction in septal wall thickness, a defining characteristic of HCM, as well as an improvement in patient reported quality of life, as measured by the Kansas City Cardiomyopathy Questionnaire were also reported.

Our second clinical-stage candidate is danicamtiv, designed to increase the contractility of the heart (systolic function) with minimal or no effect on myocardial relaxation and compliance (diastolic function) by acting directly on the proteins in the heart muscle responsible for contraction.

We recently announced interim results from a Phase 2a multiple-ascending dose clinical trial of danicamtiv, in patients with stable heart failure. This trial follows the completion of two single-ascending dose Phase 1 studies, in healthy volunteers and in patients with dilated cardiomyopathy, a disease of systolic dysfunction that can result in heart failure. After seven days of treatment with danicamtiv, the average increase in stroke volume, a measure of the amount of blood pumped from the left ventricle, was greater than 10% relative to baseline, on a placebo-adjusted basis. No impact on measures of diastolic function, or the heart's ability to relax and fill, was observed. We plan to advance danicamtiv to a Phase 2 study in patients with genetic dilated cardiomyopathy (DCM) in the second quarter of 2020.

In August 2019, we commenced dosing healthy volunteers in a Phase 1 trial of small molecule MYK-224 for the treatment of HCM. The randomized, placebo-controlled Phase 1 study is designed to evaluate the safety, tolerability, and pharmacokinetics of MYK-224. Topline results are expected in the third quarter of 2020.

Financial Overview

We have not generated net income from operations and, as of December 31, 2019, had an accumulated deficit of $478.8 million, primarily as a result of research and development and selling, general and administrative expenses. We have not generated any revenue from product sales since our inception and have funded our operations primarily through the issuance of equity securities and payments from Sanofi pursuant to the Collaboration Agreement that was terminated in December 2018. We expect to incur significant and increasing losses from operations for the foreseeable future, and we can provide no assurance that we will ever generate significant revenue or profits. As of December 31, 2019, we have cash and cash equivalents of $101.4 million, short-term investments of $314.7 million and long-term investments of $14.2 million. Net proceeds from our equity issuances since inception have totaled $797.6 million. Funds received from Sanofi in connection with the collaboration agreement have totaled $153.9 million.

On January 3, 2020, we entered into a sales agreement with a sales agent to establish an at-the-market (ATM) offering program, under which we are permitted to offer and sell, from time to time, shares of common stock having a maximum aggregate offering price of up to $200 million.

Termination of Sanofi Collaboration

Until December 31, 2018 we had an exclusive License and Collaboration Agreement (Collaboration Agreement) with Aventis Inc., a wholly-owned subsidiary of Sanofi. On December 31, 2018, Sanofi notified us of their intent to terminate our collaboration; specifically, Sanofi elected not to continue with the HCM-1 and danicamtiv programs. As a result, cost sharing and Sanofi's reimbursement of our research and development costs for mavacamten and MYK-224 ended in the first half of 2019. At that time Sanofi had continuing rights to royalties in the event of commercialization of the HCM-1 program. In July 2019, we repurchased those rights from Sanofi for $80.0 million. Neither we nor Sanofi have any material continuing rights or obligations under the Collaboration Agreement.

Components of Operating Results

Collaboration and License Revenue

We have not recorded revenues in the year ended December 31, 2019, and all revenue in the years ended December 31, 2018 and 2017 is derived from the Collaboration Agreement with Sanofi. The Collaboration Agreement provided for the research, development and potential commercialization of pharmaceutical products for the treatment, prevention and diagnosis of hypertrophic and dilated cardiomyopathy, as well as potential additional indications. Revenues for the two years ended December 31, 2018 relate to a $45.0 million payment received from Sanofi in January 2017 as a non-refundable continuation payment for such research and development. The $45.0 million was recognized pro-rata over the two-year period ending December 31, 2018 based on a cost-based input method and was recorded proportionally in relation to our research and development effort over those periods.

Operating Expenses

Research and Development Expenses

Research and development expenses consist of salaries and benefits, including stock-based compensation, lab supplies and facility costs, and fees paid to contract manufacturing organizations (CMOs) and clinical research organizations (CROs) to conduct research and development activities on our behalf. Research and development expenses are shown net of amounts that Sanofi agreed to reimburse us under the cost sharing program for research and development activities. Payments made prior to the receipt of goods or services are capitalized until the goods or services are received.

Research and development expenses incurred in the development and potential commercialization of mavacamten, danicamtiv and other product candidates, are shown net of $18.5 million, $23.1 million and $7.3 million in Sanofi research and development reimbursements during the years ended December 31, 2019, 2018 and 2017, respectively (in thousands):

	Year Ended December 31,		
	2019	2018	2017
Mavacamten	$ 72,975	$ 30,012	$ 19,902
Danicamtiv	23,197	16,583	11,286
Other	49,999	22,179	16,948
Total research and development expenses	$ 146,171	$ 68,774	$ 48,136

Selling, General and Administrative Expenses

Selling, general and administrative expenses consist principally of salaries and benefits, including stock-based compensation, professional fees for legal, consulting, audit and tax services, pre-commercial market research, rent, patient advocacy, disease education, strategic communications and other general operating expenses not otherwise classified as research and development expenses.

Interest and Other Income, Net

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

Critical Accounting Estimates

This discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles. The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, as well as the reported expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. We believe that the estimates derived from our accounting policies as discussed below are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management's judgments and estimates. In addition, refer to the notes to the financial statements contained in this Form 10-K for a complete discussion of our accounting policies.

Clinical Trials Accrued Liabilities

Our clinical trials accrued liabilities are a component of research and development expenses and based on patient enrollment and related costs at clinical investigator sites as well as estimates for the services received and efforts expended pursuant to contracts with clinical research organizations ("CROs") that conduct and manage clinical trials on our behalf. We estimate clinical trials accrued liabilities for services for which we have not yet been invoiced or otherwise notified of the actual cost based on the services performed, pursuant to contracts with research institutions and CROs that conduct and manage preclinical studies and clinical trials on our behalf. We estimate these expenses based on discussions with our internal clinical management personnel and CROs as to the progress or stage of completion of trials or services and the contracted fees to be paid for such services. Our assumptions used in developing the estimate include the progress or stage of completion and patient enrollment of the clinical trials.

Stock-Based Compensation Expense

We account for stock-based compensation arrangements with employees in accordance with ASC 718, *Stock Compensation.* ASC 718 requires the recognition of compensation expense, using a fair value-based method, for costs related to all stock-based payments including stock options. Our determination of the fair value of stock options on the date of grant utilizes the Black-Scholes option-pricing model for stock options with time-based vesting and is impacted by our common stock price as well as changes in assumptions regarding a number of highly complex and subjective variables. These variables include the expected term that options will remain outstanding, expected common stock price volatility over the term of the option awards, risk-free interest rates and expected dividends. Changes in the assumptions underlying the variables can materially affect the fair value and ultimately how much stock-based compensation expense is recognized. These inputs are subjective and generally require significant analysis and judgment to develop.

Stock-based awards granted include time-based and performance-based stock options. Stock-based compensation expense for performance stock options is based on the probability of achieving certain performance criteria, as defined in the individual option grant agreement. We estimate the number of performance options ultimately expected to vest and recognize stock-based compensation expense for those options expected to vest when it becomes probable that the performance criteria will be met.

Recent Accounting Pronouncements

The information required by this item is included in Note 2, "Summary of Significant Accounting Policies of the Notes to Consolidated Financial Statements" included in this Form 10-K.

Results of Operations

This section of this Form 10-K discusses 2019 and 2018 items and year-to-year comparisons between 2019 and 2018 results of operations. Discussions of 2017 items and year-to-year comparisons between 2018 and 2017 can be found in "Management's Discussion and Analysis of Financial Condition and Results of Operations" in Part II, Item 7 of the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2018.

Comparison of the Years Ended December 31, 2019 and 2018

The following table summarizes our results of operations during the periods indicated (in thousands):

	Year Ended December 31,			$ Change		% Change	
	2019	2018	2017	2019 vs 2018	2018 vs 2017	2019 vs 2018	2018 vs 2017
Collaboration and license revenue	$ —	$ 33,558	$ 11,442	$ (33,558)	$ 22,116	-100%	193%
Operating expenses:							
Repurchase of royalty rights	80,000	—	—	80,000	—	*	*
Research and development, net	146,171	68,774	48,136	77,397	20,638	113%	43%
Selling, general and administrative	61,663	38,435	21,973	23,228	16,462	60%	75%
Total operating expenses	287,834	107,209	70,109	180,625	37,100	168%	53%
Loss from operations	(287,834)	(73,651)	(58,667)	(214,183)	(14,984)	291%	26%
Interest and other income, net	11,621	5,953	1,657	5,668	4,296	95%	259%
Net loss	$ (276,213)	$ (67,698)	$ (57,010)	$ (208,515)	$ (10,688)	308%	19%

* Not meaningful

Collaboration and License Revenue

Collaboration and license revenue was zero and $33.6 million for the years ending December 31, 2019 and 2018, respectively. The prior year's revenue relates to the amounts recognized from the continuation payment of $45.0 million under the Collaboration Agreement, under which all revenues were recognized as of December 31, 2018.

Repurchase of Royalty Rights

In July 2019, Sanofi's continuing rights to royalties in the event of commercialization of the HCM-1 programs were terminated when we repurchased those rights for $80.0 million.

Research and Development Expenses

Research and development expenses totaled $146.2 million for the year ended December 31, 2019, an increase of $77.4 million, or 113%, from $68.8 million for the prior year. The increase in research and development expenses was primarily due to the following changes:

- $29.7 million increase in clinical expenses related to our mavacamten and danicamtiv clinical trials;
- $15.2 million increase in personnel expenses due to a higher employee headcount;
- $7.5 million increase in contract research, chemistry and biology expenses on discovery and pre-clinical programs;
- $6.5 million increase in stock compensation expense;
- $4.5 million increase in contract manufacturing;

- $3.9 million increase in other expenses, including toxicology, software, facilities and travel;
- $3.4 million increase in professional fees;
- $2.0 million increase in medical affairs expense; and
- $4.7 million decrease in research and development reimbursements from Sanofi.

Selling, General and Administrative Expenses

Selling, general and administrative expenses totaled $61.7 million for the year ended December 31, 2019, an increase of $23.2 million, or 60%, from $38.4 million for the prior year. The increase in selling, general and administrative expenses was primarily due to the following changes:

- $7.1 million increase in stock compensation expense;
- $5.1 million increase in professional fees;
- $4.9 million increase in personnel expenses due to a higher employee headcount;
- $3.1 million increase in sponsorship of cardiovascular research and education; and
- $3.0 million increase in software, facilities and other.

Interest and Other Income, Net

Interest and other income totaled $11.6 million for the year ended December 31, 2019, an increase of $5.7 million, or 95%, from $6.0 million for the prior year. The increase in interest income was primarily due to interest earned on higher invested balances during 2019.

Liquidity and Capital Resources

We consider the following when assessing our liquidity and capital resources (in thousands):

	As of December 31,	
	2019	**2018**
Cash and cash equivalents	$ 101,436	$ 246,122
Short-term investments	$ 314,691	$ 68,564
Long-term investments	$ 14,153	$ 80,148

Since inception, we have funded our operations primarily through the issuance of our equity securities and payments from Sanofi pursuant to the Collaboration Agreement, which was terminated in December 2018. All our investments are in investment-grade securities.

On January 3, 2020, we entered into a sales agreement with a sales agent to establish an at-the-market (ATM) offering program, under which we are permitted to offer and sell, from time to time, shares of common stock having a maximum aggregate offering price of up to $200 million. On March 8, 2018, we filed a Registration Statement on Form S-3ASR (2018 Shelf Registration Statement) covering the potential offering, issuance, and sale of an indeterminate amount of common stock, preferred stock, debt securities, warrants and/or units. In March 2019, we completed a follow-on offering under the 2018 Shelf Registration Statement in which we issued 5,663,750 shares of our common stock at a price of $51.00 per share, including 738,750 shares sold directly to the underwriters upon exercise of their option to purchase up to 738,750 shares of our common stock within 30 days of the offering. We received proceeds totaling approximately $271.2 million from the offering, net of underwriting discounts, commissions and offering expenses.

We believe we have sufficient financial resources to meet our business requirements for the 12 months following the date of this Annual Report on Form 10-K. We expect to incur substantial expenditures in the foreseeable future for the advancement of our precision medicine platform, the development and potential commercialization of our product candidates and the discovery, development and potential commercialization of any additional product candidates we may pursue. Furthermore, if our clinical trials for mavacamten are successful, or our other product candidates, including danicamtiv, enter into late-stage clinical trials or more advanced discovery and development stages, we may need to raise additional capital in order to further advance our product candidates towards regulatory approval.

Contractual Obligations and Commitments

Purchase Commitments

We conduct product research and development programs through a combination of internal and collaborative programs that include, among others, arrangements with universities, CROs and clinical research sites. We have contractual arrangements with these organizations; however, these contracts are generally cancelable on 30 days' notice and the obligations under these contracts are largely based on services performed.

Facility Leases

Information regarding our facility leases is contained in Note 6 "Leases" in our consolidated financial statements included in this Form 10-K.

Future annual minimum lease payments due under the new and existing operating leases at December 31 of each year are as follows (in thousands):

	Payments due by period				
	Less than 1 year	1 to 3 years	3 to 5 years	After 5 years	Total
Lease obligations, net	$ 5,840	$ 17,218	$ 18,444	$ 52,064	$ 93,566

Cash Flows

The following table sets forth the primary sources and uses of cash for each of the periods presented below (in thousands):

	Year Ended December 31,		
	2019	2018	2017
Net cash (used in) provided by:			
Operating activities	$ (241,769)	$ (64,815)	$ (9,838)
Investing activities	(181,161)	(99,848)	(37,551)
Financing activities	278,295	188,071	136,189
Net (decrease) increase in cash, cash equivalents and restricted cash	$ (144,635)	$ 23,408	$ 88,800

Cash Used in Operating Activities

Cash used in operating activities was $241.8 million for the year ending December 31, 2019, driven primarily by a net loss of $276.2 million, adjusted for non-cash stock-based compensation of $33.0 million and depreciation of $1.9 million. Other changes in cash resulted from a decrease in prepayments from Sanofi of $13.0 million, an increase in prepaid expenses and other current assets of $2.6 million, offset by an increase in accrued liabilities of $11.7 million and an increase in accounts payable of $3.1 million.

Cash used in operating activities was $64.8 million for the year ending December 31, 2018, driven primarily by a net loss of $67.7 million, adjusted for non-cash stock-based compensation of $19.3 million and depreciation of $1.6 million. Other changes in cash resulted from a decrease in deferred revenue of $33.6 million, a decrease in prepaid expenses and other current assets of $2.9 million, offset by increases in prepayments from Sanofi of $8.5 million and increases in accrued liabilities of $9.1 million.

Cash used in operating activities was $9.8 million for the year ended December 31, 2017, driven primarily by a net loss of $57.0 million, as adjusted for the implementation of ASC 606, "Revenues from Contracts with Customers", adjusted for non-cash stock-based compensation of $6.1 million and depreciation of $1.3 million. Other changes in cash resulted from a decrease of receivables from Sanofi of $44.0 million, prepayment of $4.4 million from Sanofi towards registration program costs under the HCM-1 reimbursement program and an increase in accrued liabilities of $3.0 million, offset by a decrease in deferred revenue of $11.4 million related to the $25.0 million continuation payment under the Sanofi Collaboration Agreement.

Cash Used in Investing Activities

Cash used in investing activities totaled $188.1 million for the year ending December 31, 2019 and consisted of purchases of investments of $259.9 million and purchases of lab and office equipment of $3.3 million, offset by $4.0 million and $78.0 million in sales and maturities of investments, respectively.

Cash used in investing activities totaled $99.8 million for the year ending December 31, 2018 and consisted of purchases of investments of $132.5 million and purchases of lab and office equipment of $3.4 million, offset by $8.0 million and $28.0 million in sales and maturities of investments, respectively.

Cash used in investing activities was $37.6 million for the year ended December 31, 2017 and consisted of purchases of investments of $44.0 million and purchases of lab and office equipment of $1.5 million, offset by sales and maturities of investments of $8.0 million.

Cash Provided by Financing Activities

Cash provided by financing activities in the year ended December 31, 2019 totaled $278.3 million and was provided by $271.2 million in proceeds from public offering of our common stock during the year, net of issuance costs, and $7.1 million in proceeds from the exercise of stock options and purchases under the employee stock purchase plan.

Cash provided by financing activities in the year ended December 31, 2018 totaled $188.1 million and was provided by $181.9 million in proceeds from public offering of our common stock during the year, net of issuance costs, and $6.2 million in proceeds from the exercise of stock options and purchases under the employee stock purchase plan.

Cash provided by financing activities in the year ended December 31, 2017 was $136.2 million consisting of net proceeds of $133.9 million received from the public offering of our common stock in August 2017 and $2.4 million in proceeds from the exercise of stock options and purchases under the employee stock purchase plan.

Off-Balance Sheet Arrangements

Since our inception, we have not engaged in any off-balance sheet arrangements, as defined in the rules and regulations of the SEC. See Note 7 “Commitments and Contingencies”, in our consolidated financial statements appearing in this Form 10-K regarding our guarantees and indemnifications.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

The market risk inherent in our financial instruments represents the potential loss arising from adverse changes in interest rates or exchange rates. As of December 31, 2019, we had cash, cash equivalents and short-term and long-term investments of $430.3 million, consisting of interest-bearing money market accounts and money market funds, which would be affected by changes in the general level of United States interest rates. However, due to the short-term maturities of our cash and cash equivalents and the low- risk profile of our investments, an immediate 100 basis point change in interest rates would not have a material effect on the fair value of our cash, cash equivalents or investments.

We are also exposed to foreign currency exchange rate risk inherent in our contracts with research institutions and certain contract research organizations, as certain services are performed by them outside the United States. We make payments in Euros and Australian dollars to international vendors. A significant movement in the Euro or Australian dollar may have a material impact on our financial position in the future.

We do not believe that inflation, interest rate changes or exchange rate fluctuations had a significant impact on our results of operations for any periods presented.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

Our consolidated financial statements and supplementary data and the report of our independent registered public accounting firm are included in Item 15 of this Annual Report on Form 10-K on pages F-1 through F-25.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures

The term “disclosure controls and procedures,” as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, refers to controls and procedures that are designed to provide reasonable assurance that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC’s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to provide reasonable assurance that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company’s management, including its principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our disclosure controls and procedures are designed to provide reasonable assurance of achieving their control objectives.

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer, has evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2019, the end of the period covered by this Annual Report on Form 10-K. Based upon such evaluation, our Chief Executive Officer and Principal Financial and Accounting Officer have concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of such date.

Management’s Annual Report on Internal Control Over Financial Reporting

The Company’s management is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) of the Exchange Act). Internal control over financial reporting is a process designed under the supervision and with the participation of our management, including the individuals serving as our principal executive officer and principal financial and accounting officer, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. Management conducted an assessment of the effectiveness of the Company’s internal control over financial reporting based on the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in Internal Control “Internal Control - Integrated Framework” (2013 Framework). Based on this assessment, our management concluded that, as of December 31, 2019, the Company’s internal control over financial reporting was effective based on those criteria. The effectiveness of our internal control over financial reporting as of December 31, 2019 has been audited by PricewaterhouseCoopers LLP, an independent registered public accounting firm as stated in its report which is included in this Form 10-K.

Changes in Internal Control Over Financial Reporting

There has been no change in our internal control over financial reporting during the quarter ended December 31, 2019, that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

None.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

Except as set forth below, the information required by this item will be contained in our definitive proxy statement to be filed with the SEC in connection with the Annual Meeting of Stockholders within 120 days after the conclusion of our fiscal year ended December 31, 2019, or the Proxy Statement, and is incorporated in this Annual Report on Form 10-K by reference.

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. A current copy of the code is posted on the Corporate Governance section of our website, which is located at www.myokardia.com. If we make any substantive amendments to, or grant any waivers from, the code of business conduct and ethics for our principal executive officer, principal financial officer, principal accounting officer, controller or persons performing similar functions, or any officer or director, we will disclose the nature of such amendment or waiver on our website or in a current report on Form 8-K.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this item will be contained in the Proxy Statement and is incorporated in this Annual Report on Form 10-K by reference.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information required by this item will be contained in the Proxy Statement and is incorporated in this Annual Report on Form 10-K by reference.

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

The information required by this item will be contained in the Proxy Statement and is incorporated in this Annual Report on Form 10-K by reference.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

The information required by this item will be contained in the Proxy Statement and is incorporated in this Annual Report on Form 10-K by reference.

PART IV

ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES

(a) The following documents are filed as part of this report:

(1) FINANCIAL STATEMENTS

Financial Statements—See Index to Consolidated Financial Statements at Item 8 of this Annual Report on Form 10-K, beginning on page F-1.

(2) FINANCIAL STATEMENT SCHEDULES

Financial statement schedules have been omitted in this Annual Report on Form 10-K because they are not applicable, not required under the instructions, or the information requested is set forth in the consolidated financial statements or related notes thereto.

(b) Exhibits. See Item 15(b) below for a complete list of Exhibits to this report.

EXHIBIT INDEX

Exhibit Number	Exhibit Title	Incorporated by Reference			Filing Date
		Form	File No.	Exhibit	
3.1	Restated Certificate of Incorporation of the Registrant	10-Q	001-37609	3.1	November 18, 2015
3.2	Amended and Restated Bylaws of the Registrant	S-1/A	333-207151	3.4	October 13, 2015
4.1	Specimen Common Stock Certificate	S-1/A	333-207151	4.1	October 19, 2015
4.2	Description of Securities	—	—	—	Filed herewith
10.1#	2012 Equity Incentive Plan and forms of award agreements thereunder	S-1	333-207151	10.1	September 28, 2015
10.2#	2015 Stock Option and Incentive Plan and forms of award agreements thereunder	S-1/A	333-207151	10.2	October 19, 2015
10.3#	Employment Offer Letter Agreement, by and between the Registrant and Robert S. McDowell, Ph.D., dated June 8, 2012	S-1	333-207151	10.3	September 28, 2015
10.4#	Employment Offer Letter Agreement, by and between the Registrant and T. Anastasios Gianakakos, dated September 19, 2013	S-1	333-207151	10.4	September 28, 2015
10.5#	Employment Offer Letter Agreement, by and between the Registrant and Jacob Bauer, dated July 2, 2014	S-1	333-207151	10.5	September 28, 2015
10.6#	Employment Offer Letter Agreement, by and between the Registrant and William Fairey, dated January 5, 2019	10-K	001-37609	10.6	February 28, 2019
10.7	Lease Agreement, by and between the Registrant and HCP LS Redwood City, LLC, dated September 15, 2014	S-1	333-207151	10.9	September 28, 2015
10.8#	Form of Indemnification Agreement, by and between the Registrant and each of its directors and officers	S-1/A	333-207151	10.11	October 13, 2015
10.9#	2015 Employee Stock Purchase Plan	S-1/A	333-207151	10.14	October 19, 2015
10.10#	Change in Control and Severance Policy	10-K	001-37609	10.12	February 28, 2019
10.11#	Amended and Restated Non-Employee Director Compensation Policy	10-K	001-37609	10.13	February 28, 2019
10.12#	Senior Executive Cash Incentive Bonus Plan	8-K	001-37609	10.1	February 5, 2016
10.13#	Employment Offer Letter Agreement by and between the Registrant and Cynthia Ladd, dated December 4, 2017.	10-K	001-37609	10.17	March 8, 2018
10.16#	Employment Offer Letter Agreement by and between the Registrant and Taylor Harris, dated March 26, 2018.	8-K	001-37609	10.1	April 4, 2018

Exhibit Number	Exhibit Title	Incorporated by Reference			Filing Date
		Form	File No.	Exhibit	
10.17	Lease by and between the Registrant and HCP LS Brisbane, LLC dated September 13, 2018.	10-Q	001-37609	10.1	November 8, 2018
10.18	Lease by and between the Registrant and Kashiwa Fudosan America, Inc. dated October 22, 2018.	10-K	001-37609	10.22	February 28, 2019
10.19†	Termination Agreement, by and between the Registrant and Aventis, Inc. dated July 17, 2019.	10-Q	001-37609	10.1	November 4, 2019
10.20#	Transition Agreement, by and between the Registrant and June Lee dated October 4, 2019.	10-Q	001-37609	10.2	November 4, 2019
10.21	Common Stock Sales Agreement, by and between the Registrant and Cowen and Company, LLC dated January 3, 2020.	8-K	001-37609	1.1	January 3, 2020
21.1	List of Subsidiaries	—	—	—	Filed herewith
23.1	Consent of independent registered public accounting firm	—	—	—	Filed herewith
24.1	Power of attorney (included on signature page to this Annual Report)	—	—	—	Filed herewith
31.1	Certification of Principal Executive Officer of the Registrant, as required by Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	—	—	—	Filed herewith
31.2	Certification of Principal Financial Officer of the Registrant, as required by Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	—	—	—	Filed herewith
32.1	Certification by the Principal Executive Officer, as required by Rule 13a-14(b) or Rule 15d-14(b) and Section 1350 of Chapter 36 of Title 18 of the United States Code (18 U.S.C. §1350).	—	—	—	Filed herewith
32.2	Certification by the Principal Financial Officer, as required by Rule 13a-14(b) or Rule 15d-14(b) and Section 1350 of Chapter 36 of Title 18 of the United States Code (18 U.S.C. §1350).	—	—	—	Filed herewith
101.SCH	Inline XBRL Taxonomy Extension Schema Document	—	—	—	Filed herewith
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document	—	—	—	Filed herewith
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document	—	—	—	Filed herewith
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document	—	—	—	Filed herewith
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document	—	—	—	Filed herewith
104	Cover Page Interactive Data File (formatted as inline XBRL with applicable taxonomy extension information contained in Exhibits 101.*)	—	—	—	Filed herewith

† Portions of this exhibit have been omitted as confidential information.
# Represents management compensation plan, contract or arrangement.

ITEM 16. FORM 10-K SUMMARY

None.

MYOKARDIA, INC.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of MyoKardia, Inc.

Opinions on the Financial Statements and Internal Control over Financial Reporting

We have audited the accompanying consolidated balance sheets of MyoKardia, Inc. and its subsidiaries (the "Company") as of December 31, 2019 and 2018, and the related consolidated statements of operations and comprehensive loss, of stockholders' equity and of cash flows for each of the three years in the period ended December 31, 2019, including the related notes (collectively referred to as the "consolidated financial statements"). We also have audited the Company's internal control over financial reporting as of December 31, 2019, based on criteria established in Internal Control - Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2019 and 2018, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2019 in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2019, based on criteria established in Internal Control - Integrated Framework (2013) issued by the COSO.

Basis for Opinions

The Company's management is responsible for these consolidated financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in Management's Annual Report on Internal Control Over Financial Reporting appearing under Item 9A. Our responsibility is to express opinions on the Company's consolidated financial statements and on the Company's internal control over financial reporting based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the consolidated financial statements included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

Definition and Limitations of Internal Control over Financial Reporting

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

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

Critical Audit Matters

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

Clinical trials accrued liabilities

As described in Notes 2 and 5 to the consolidated financial statements, the Company recorded $11.5 million in clinical trials accrued liabilities as of December 31, 2019. The Company's clinical trials accrued liabilities are a component of research and development expenses and based on patient enrollment and related costs at clinical investigator sites as well as estimates for the services received and efforts expended pursuant to contracts with clinical research organizations ("CROs") that conduct and manage clinical trials on the Company's behalf. Management estimates clinical trials accrued liabilities for services the Company has not yet been invoiced or otherwise notified of the actual cost based on the services performed, pursuant to contracts with research institutions and CROs that conduct and manage preclinical studies and clinical trials on its behalf. Management estimates these expenses based on discussions with the Company's internal clinical management personnel and CROs as to the progress or stage of completion of trials or services and the contracted fees to be paid for such services. Assumptions used by management in developing the estimate include the progress or stage of completion and patient enrollment of the clinical trials.

The principal considerations for our determination that performing procedures relating to clinical trials accrued liabilities is a critical audit matter are there was significant judgment by management in estimating the clinical trials expenses incurred to date for services which the Company has not yet been invoiced or otherwise notified of actual cost, which are based on progress or stage of completion patient enrollment of the clinical trials. This in turn led to a high degree of auditor judgment, subjectivity and effort in performing procedures and evaluating audit evidence relating to expense estimates made by management to establish clinical trials accrued liabilities.

Addressing the matter involved performing procedures and evaluating audit evidence in connection with forming our overall opinion on the consolidated financial statements. These procedures included testing the effectiveness of controls relating to the clinical trials accrued liabilities, including the review and approval of assumptions used to estimate clinical trials accruals, such as, progress or stage of completion and patient enrollment of the clinical trials. These procedures also included, among others, (1) testing management's process for estimating clinical trials accrued liabilities, (2) evaluating the appropriateness of the approach used by management to develop the estimate, (3) evaluating the reasonableness of significant assumptions, including the progress or stage of completion and patient enrollment of the clinical trials, (4) testing the completeness and accuracy of the data inputs to the approach, (5) confirming clinical costs and contracted fees with the CROs on a test basis, and (6) examining CRO contracts on a test basis to evaluate the completeness of costs considered in the estimate.

/s/ PricewaterhouseCoopers LLP
San Jose, California
February 27, 2020

We have served as the Company's auditor since 2014.

MYOKARDIA, INC.

Consolidated Balance Sheets
(In thousands, except share and per share amounts)

	December 31, 2019	December 31, 2018
Assets		
Current assets		
Cash and cash equivalents	$ 101,436	$ 246,122
Short-term investments	314,691	68,564
Prepaid expenses and other current assets	7,709	4,760
Total current assets	423,836	319,446
Property and equipment, net	15,743	5,138
Operating lease right-of-use assets	417	—
Long-term investments	14,153	80,148
Restricted cash and other	1,945	2,521
Total assets	$ 456,094	$ 407,253
Liabilities and stockholders' equity		
Current liabilities		
Accounts payable	$ 6,237	$ 2,946
Accrued liabilities	41,292	20,758
Prepayment from collaboration partner	—	12,973
Operating lease liabilities - current	383	—
Total current liabilities	47,912	36,677
Other long-term liabilities	1,908	9
Total liabilities	49,820	36,686
Commitments and contingencies (Note 7)		
Stockholders' equity		
Preferred stock, $0.0001 par value; 5,000,000 shares authorized; none issued and outstanding	—	—
Common stock, $0.0001 par value, 150,000,000 shares authorized at December 31, 2019 and 2018; 46,379,073 and 40,288,949 shares issued and outstanding at December 31, 2019 and 2018, respectively	5	4
Additional paid-in capital	884,486	573,183
Accumulated other comprehensive income (loss)	549	(67)
Accumulated deficit	(478,766)	(202,553)
Total stockholders' equity	406,274	370,567
Total liabilities and stockholders' equity	$ 456,094	$ 407,253

The accompanying notes are an integral part of these Consolidated Financial Statements

MYOKARDIA, INC.

Consolidated Statements of Operations and Comprehensive Loss
(In thousands, except share and per share amounts)

	Year Ended December 31,		
	2019	2018	2017
Collaboration and license revenue	$ —	$ 33,558	$ 11,442
Operating expenses:			
Repurchase of royalty rights	80,000	—	—
Research and development	146,171	68,774	48,136
Selling, general and administrative	61,663	38,435	21,973
Total operating expenses	287,834	107,209	70,109
Loss from operations	(287,834)	(73,651)	(58,667)
Interest and other income, net	11,621	5,953	1,657
Net loss	(276,213)	(67,698)	(57,010)
Other comprehensive income (loss)	616	125	(200)
Comprehensive loss	$ (275,597)	$ (67,573)	$ (57,210)
Net loss per share, basic and diluted	$ (6.17)	$ (1.76)	$ (1.74)
Weighted average number of shares used to compute net loss per share, basic and diluted	44,765,496	38,386,906	32,832,514

The accompanying notes are an integral part of these Consolidated Financial Statements

MYOKARDIA, INC.

Consolidated Statements of Stockholders' Equity
(In thousands, except share amounts)

	Common Stock		Additional Paid-In Capital	Accumulated other comprehensive income/ (loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
BALANCE—December 31, 2016	31,428,998	$ 3	$ 223,208	$ 8	$ (77,837)	$ 145,382
Issuance of common stock in connection with the 2017 follow-on offering, net of issuance costs of $9,025	4,025,000	1	133,861	—	—	133,862
Issuance of common stock under equity incentive and employee stock purchase plans	400,754	—	2,365	—	—	2,365
Repurchase of early exercised stock options	(41,961)	—	(45)	—	—	(45)
Vesting of early exercised stock options and restricted stock	—	—	184	—	—	184
Stock-based compensation	—	—	6,138	—	—	6,138
Cumulative effect adjustment upon adoption of ASU 2016-09	—	—	8	—	(8)	—
Unrealized losses	—	—	—	(200)	—	(200)
Net loss	—	—	—	—	(57,010)	(57,010)
BALANCE—December 31, 2017	35,812,791	$ 4	$ 365,719	$ (192)	$ (134,855)	$ 230,676
Issuance of common stock in connection with the 2018 follow-on offering, net of issuance costs of $12,233	3,961,147	—	181,863	—	—	181,863
Issuance of common stock under equity incentive and employee stock purchase plans	516,008	—	6,208	—	—	6,208
Repurchase of early exercised stock options	(997)	—	(1)	—	—	(1)
Vesting of early exercised stock options and restricted stock	—	—	53	—	—	53
Stock-based compensation	—	—	19,341	—	—	19,341
Unrealized gains	—	—	—	125	—	125
Net loss	—	—	—	—	(67,698)	(67,698)
BALANCE—December 31, 2018	40,288,949	4	573,183	(67)	(202,553)	370,567
Issuance of common stock in connection with the 2019 follow-on offering, net of issuance costs of $17,638	5,663,750	1	271,223	—	—	271,224
Issuance of common stock under equity incentive and employee stock purchase plans	426,374	—	7,071	—	—	7,071
Vesting of early exercised stock options and restricted stock	—	—	15	—	—	15
Stock-based compensation	—	—	32,994	—	—	32,994
Unrealized gains	—	—	—	616	—	616
Net loss	—	—	—	—	(276,213)	(276,213)
BALANCE—December 31, 2019	46,379,073	$ 5	$ 884,486	$ 549	$ (478,766)	$ 406,274

The accompanying notes are an integral part of these Consolidated Financial Statements

MYOKARDIA, INC.

Consolidated Statements of Cash Flows
(In thousands)

	Year Ended December 31,		
	2019	**2018**	**2017**
Cash flow from operating activities:			
Net loss	$ (276,213)	$ (67,698)	$ (57,010)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation expense	32,994	19,341	6,138
Depreciation	1,948	1,567	1,294
Amortization of discount on investments	(1,619)	(279)	85
Loss on disposal of equipment	—	—	4
Change in operating assets and liabilities:			
Receivable from collaboration partner	—	1,013	43,987
Prepaid expenses and other current assets	(2,612)	(2,884)	(482)
Operating lease right-of-use assets	2,618	—	—
Other long-term assets	290	(296)	(59)
Accounts payable	3,064	671	367
Accrued liabilities	11,665	8,945	2,968
Prepayment from collaboration partner	(12,973)	8,541	4,432
Operating lease liabilities	(2,838)	—	—
Other long-term liabilities	1,907	(178)	(120)
Deferred revenue	—	(33,558)	(11,442)
Net cash used in operating activities	(241,769)	(64,815)	(9,838)
Cash flow from investing activities:			
Purchases of investments	(259,897)	(132,475)	(44,044)
Sales of investments	4,000	8,000	4,000
Maturities of investments	78,000	28,000	4,000
Purchases of property and equipment	(3,264)	(3,373)	(1,517)
Proceeds from sale of equipment	—	—	10
Net cash used in investing activities	(181,161)	(99,848)	(37,551)
Cash flow from financing activities:			
Proceeds from issuance of common stock in follow-on offerings, net of issuance and financing costs	271,224	181,863	133,862
Proceeds from exercise of stock options and employee stock purchase plan	7,071	6,208	2,365
Payments of prior period offering costs	—	—	(38)
Net cash provided by financing activities	278,295	188,071	136,189
Net (decrease) increase in cash, cash equivalents and restricted cash	(144,635)	23,408	88,800
Cash, cash equivalents and restricted cash, beginning of period	248,265	224,857	136,057
Cash, cash equivalents and restricted cash, end of period	$ 103,630	$ 248,265	$ 224,857
Non-cash investing and financing activities:			
Vesting of early exercised options and restricted stock	$ 15	$ 53	$ 184
Unpaid portion of property and equipment purchases included in period-end accounts payable and accrued liabilities	$ 9,756	$ 468	$ 283

The accompanying notes are an integral part of these Consolidated Financial Statements

1. Organization

MyoKardia, Inc. (the Company) is a clinical-stage biopharmaceutical company pioneering a precision medicine approach to discover, develop and commercialize targeted therapies for the treatment of serious and neglected rare cardiovascular diseases. The Company's initial focus is on the treatment of cardiomyopathies, a group of diseases of the heart muscle. MyoKardia's pipeline includes mavacamten and MYK-224, which are being studied for the treatment of hypertrophic cardiomyopathy, LUS-1, being studied for the treatment of diseases of diastolic dysfunction and danicamtiv (formerly MYK-491) and ACT-1, being studied for the treatment of diseases of systolic dysfunction.

MyoKardia's most advanced programs are: mavacamten, which is in four clinical trials including a Phase 3 study in patients with hypertrophic cardiomyopathy (HCM); danicamtiv, which recently completed a Phase 2a multiple-ascending dose study in patients with stable systolic heart failure and is being advanced to a Phase 2 study in patients with genetic dilated cardiomyopathy; and MYK-224, which is in a Phase 1 randomized, placebo-controlled study in healthy volunteers.

The Company was incorporated on June 8, 2012 in Delaware. As of December 31, 2019, its corporate headquarters and operations were located in South San Francisco, California and as of the date of this filing its corporate headquarters and operations are located in Brisbane, California.

Liquidity

The Company has incurred significant operating losses since inception and has an accumulated deficit of $478.8 million as of December 31, 2019. The Company has relied on its ability to fund its operations through private and public equity financings and to a lesser extent, through a license and collaboration arrangement with a collaboration partner, Sanofi S.A. (Sanofi) via its subsidiary, Aventis, Inc. As discussed further in Note 3, the collaboration agreement ended on December 31, 2018 and the Company had no revenues relating to its Sanofi collaboration in 2019, nor has it received reimbursements of research and development expenses after June 30, 2019. The Company has not yet received regulatory approval to commercialize or sell any product and does not have customers. Management expects operating losses and negative operating cash flows to continue for the foreseeable future. As the Company continues to incur losses, a transition to profitability is dependent upon the successful development, approval, and commercialization of the Company's products and product candidates and the achievement of a level of revenues adequate to support its cost structure. The Company's ultimate success depends on the outcome of its research and development activities and anticipates the need to raise additional capital to fully implement its business plan. The Company intends to raise such capital through the issuance of additional equity, debt and/or strategic alliances with partner companies. There is no assurance that such financing will be available or that such strategic alliances will be executed, on terms acceptable to the Company, or at all.

As of December 31, 2019, the Company had $430.3 million of cash, cash equivalents and short and long-term investments, which management believes will be sufficient to meet the Company's anticipated operating and capital expenditure requirements for the twelve months following the date of issuance of these financial statements. Management's belief with respect to its ability to fund operations is based on estimates that are subject to risks and uncertainties. If actual results are different from management's estimates, the Company may need to seek additional funding.

2. Summary of Significant Accounting Policies

Basis of Presentation and Consolidation

The consolidated financial statements of the Company include the Company's accounts and have been prepared in conformity with accounting principles generally accepted in the United States of America (US GAAP) and include the Company's accounts and those of its wholly-owned subsidiaries MyoKardia Australia Pty Ltd and MyoKardia Netherlands B.V. The consolidated financial statements include the Company's accounts and those of its wholly-owned subsidiaries. All intercompany accounts, transactions and balances have been eliminated during consolidation. The functional and reporting currency of the Company and its subsidiaries is the United States Dollar.

Use of Estimates

The preparation of consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, disclosure of contingent assets and liabilities and the reported amounts of revenues and expenses in the consolidated financial statements and the accompanying notes. On an ongoing basis, management evaluates its estimates, including those related to clinical trials accrued liabilities, income tax valuation allowance and stock-based compensation. Management bases its estimates on historical experience and on various other market-specific and relevant assumptions that management believes to be reasonable under the circumstances. Actual results could differ from those estimates.

Segments

The Company operates and manages its business as one reportable and operating segment, which is the business of developing and commercializing therapeutics. The Company's chief executive officer, who is the chief operating decision maker, reviews financial information on an aggregate basis for purposes of allocating and evaluating financial performance. All revenues have been earned in the United States of America and all long-lived assets are maintained in the United States of America.

Cash and Cash Equivalents

Cash and cash equivalents consist of cash and other highly liquid investments with original maturities of three months or less from the date of purchase. At December 31, 2019 and 2018, the Company's cash and cash equivalents were comprised of funds held in checking accounts, interest-bearing money market accounts, money market funds and commercial paper.

Reconciliation of Cash, Cash Equivalents, and Restricted Cash as Reported in Consolidated Statements of Cash Flows

Cash as reported in the consolidated statements of cash flows includes the aggregate amounts of cash, cash equivalents and restricted cash as presented on the consolidated balance sheets. Restricted cash at December 31, 2019 and 2018 represents cash balances held as security in connection with the Company's facility lease agreements. The following table provides a reconciliation of cash, cash equivalents, and restricted cash within the consolidated balance sheets to the total shown in the consolidated statements of cash flows (in thousands):

	As of December 31,	
	2019	2018
Cash and cash equivalents	$ 101,436	$ 246,122
Restricted cash included in prepaid expenses and other current assets	337	—
Restricted cash included in restricted cash and other	1,857	2,143
Total cash, cash equivalents and restricted cash shown in the consolidated statements of cash flows	$ 103,630	$ 248,265

Concentration of Credit Risk

Financial instruments that potentially subject the Company to a concentration of credit risk consist of cash, cash equivalents and investments. All of the Company's cash and cash equivalents are held at financial institutions that management believes are of high credit quality. Such deposits may, at times, exceed federally insured limits. The Company invests in a variety of financial instruments, such as, but not limited to, corporate debt and United States Treasury and Government agency securities, and by policy, limits the amount of credit exposure with any one financial institution or commercial issuer. The Company has not experienced any credit losses on its investments.

Revenue Recognition

The Company did not recognize revenues during the year ended December 31, 2019. As discussed in Note 3, in the years ended December 31, 2018 and 2017 the Company generated revenue from its collaboration and license agreement with its former collaboration partner, Sanofi. The collaboration and license agreement included non-refundable upfront license fees, reimbursement of research and development costs and contingent consideration payments based on the achievement of defined collaboration objectives. To date, the Company has not recognized revenue from sales of its product candidates.

Effective January 1, 2018, the Company adopted Accounting Standards Codification Topic 606, *Revenue from Contracts with Customers* (ASC 606) using the full retrospective transition method. This standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, certain collaboration arrangements and financial instruments. Under ASC 606, the Company recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the Company expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that the Company determines are within the scope of ASC 606, the Company performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the Company satisfies a performance obligation. The Company only applies the five-step model to contracts when it is probable that Company will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within each contract and determines those that are performance obligations and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

Research and Development Expenses

Research and development costs are expensed as incurred and consist of salaries and benefits, lab supplies and facility costs, and fees paid to others that conduct certain research and development activities on the Company's behalf. Under the terms of the Company's collaboration agreement with Sanofi, which terminated effective December 31, 2018, and as discussed in Note 3, the Company and Sanofi shared qualified research and development expenses that were jointly incurred to develop certain of the Company's product candidates. Qualified costs consisted of internal and external research and development expenses including employee costs and direct out-of-pocket costs that were specifically identifiable or reasonably and directly related to the development of these candidates. Examples of qualified costs included those incurred for clinical trials, preparation for regulatory approval, manufacture or purchase of product for use in trials.

Clinical Trials Accrued Liabilities

The Company's clinical trials accrued liabilities are a component of research and development expenses and based on patient enrollment and related costs at clinical investigator sites as well as estimates for the services received and efforts expended pursuant to contracts with clinical research organizations (CROs) that conduct and manage clinical trials on the Company's behalf. Management estimates clinical trials accrued liabilities for services the Company has not yet been invoiced or otherwise notified of the actual cost based on the services performed, pursuant to contracts with research institutions and CROs that conduct and manage preclinical studies and clinical trials on its behalf. Management estimates these expenses based on discussions with the Company's internal clinical management personnel and CROs as to the progress or stage of completion of trials or services and the contracted fees to be paid for such services. Assumptions used by management in developing the estimate include the progress or stage of completion and patient enrollment of the clinical trials.

Recently Adopted Accounting Pronouncements – Leases

Effective January 1, 2019, the Company adopted Accounting Standards Codification Topic 842, Leases (ASC 842), which requires lessees to recognize a right-of-use asset (ROU) and a lease liability on the balance sheet for all leases except for short-term leases with a lease term of twelve months or less. For lessees, leases continue to be classified as either operating or finance leases in the income statement. Lessor accounting is similar to the prior model but updated to align with certain changes to the lessee model. Lessors continue to classify leases as operating, direct financing or sales-type leases. The Company elected to adopt ASC 842 under the transition method that allows for the application of the new guidance at the beginning of the adoption period without recasting comparative periods. The Company also elected transition practical expedients to the implementation of the lease standard, as follows: (1) the Company did not reassess whether any expired or existing contracts, which had commenced before January 1, 2019, the date of adoption, are or contain leases (2) the Company did not reassess the lease classification for any expired or existing leases and (3) the Company did not reassess the initial direct costs for any existing leases.

All of the Company's leases are operating leases for property, which historically have been accounted for as operating leases, and under ASC 842 were also determined to be operating leases. The Company also reviewed its open contracts as of the date of adoption and determined that none had terms and conditions that would represent ROU assets or liabilities that would be considered embedded leases.

Upon adoption, the Company recognized ROU assets and related lease liabilities totaling $2.1 million, representing the present value of future lease payments of each lease utilizing the Company's incremental borrowing rate (IBR), which is the estimated borrowing rate of a collateralized loan over the remaining term of the lease. A deferred rent amount of $0.2 million as of December 31, 2018 was also reclassified to the ROU assets, reducing the carrying value to $1.9 million.

Recently Adopted Accounting Pronouncements – Other

In December 2019, the FASB issued ASU 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes*, which removes certain exceptions for recognizing deferred taxes for investments, performing intraperiod allocation and calculating income taxes in interim periods. The ASU also adds guidance to reduce complexity in certain areas, including recognizing deferred taxes for tax goodwill and allocating taxes to members of a consolidated group. This amendment is effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2020. Early adoption is permitted. The Company adopted this amendment in December 2019 and the adoption did not have a material impact to the Company's financial statements.

In June 2018, the FASB issued ASU No. 2018-07 (Topic 718), *Compensation – Stock Compensation (ASU 2018-07)*. The update represents an expansion of Topic 718 to include share-based payment transactions for acquiring goods and services from nonemployees. An entity should apply the requirements of Topic 718 to nonemployee awards except for specific guidance on inputs to an option pricing model and the attribution of cost (that is, the period of time over which share-based payment awards vest and the pattern of cost recognition over that period). The amendments specify that Topic 718 applies to all share-based payment transactions in which a grantor acquires goods or services to be used or consumed in a grantor's own operations by issuing share-based payment awards. The amendments also clarify that Topic 718 does not apply to share-based payments used to effectively provide (1) financing to the issuer or (2) awards granted in conjunction with selling goods or services to customers as part of a contract accounted for under Topic 606, Revenue from Contracts with Customers. The Company adopted ASU 2018-17 in the first quarter of 2019 and the adoption of this standard did not have a material impact to the Company's financial statements.

In February 2018, the FASB issued ASU No. 2018-05 (Topic 740) *Income Taxes*, Amendments to SEC Paragraphs Pursuant to SEC Staff Accounting Bulletin No. 118. The update provides guidance that gives entities the option to reclassify to retained earnings tax effects related to items in accumulated other comprehensive income (OCI) that the FASB refers to as having been stranded in accumulated OCI as a result of tax reform. Entities can early adopt the guidance in any interim or annual period for which financial statements have not yet been issued and apply it either (1) in the period of adoption or (2) retrospectively to each period in which the income tax effects of the Tax Cuts and Jobs Act related to items in accumulated OCI are recognized. The Company adopted ASU 2018-05 in the first quarter of 2019 utilizing the modified retrospective transition method. The adoption of this standard did not have a material impact to the Company's financial statements.

Recently Issued Accounting Pronouncements Not Yet Adopted

In November 2018, the FASB issued ASU 2018-18 (Topic 808), Clarifying the Interaction Between Topic 808 and Topic 606, which provides guidance on how to assess whether certain transactions between collaborative arrangement participants should be accounted for within the revenue recognition standard. The ASU also provides more comparability in the presentation of revenue for certain transactions between collaborative arrangement participants. It accomplishes this by allowing organizations to only present units of account in collaborative arrangements that are within the scope of the revenue recognition standard together with revenue accounted for under the revenue recognition standard. The parts of the collaborative arrangement that are not in the scope of the revenue recognition standard should be presented separately from revenue accounted for under the revenue recognition standard. For public companies, the amendments in ASU 2018-18 are effective for fiscal years beginning after December 15, 2019, and interim periods within those fiscal years. Early adoption is permitted. The Company has evaluated this amendment and it is not expected to have a material impact to the Company's financial statements.

In August 2018, the FASB issued ASU 2018-13 (Topic 820), *Fair Value Measurement*, which modifies the disclosure requirements in Topic 820 by removing requirements for disclosing (i) amounts of and reasons for transfers between the Level 1 and Level 2 hierarchies, (ii) the policy for timing of transfers between levels and (iii) the valuation processes for Level 3 fair value measurements. The ASU 2018-13 amendment also adds requirements for disclosure of changes in unrealized gains and losses for the period relating to Level 3 fair value measurements and other factors considered in the valuation of Level 3 investments. This amendment is effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2019. The Company has evaluated this amendment and it is not expected to have a material impact to the Company's financial statements.

In June 2016, the FASB issued ASU No. 2016-13 (Topic 326), *Financial Instruments –Measurement of Credit Losses on Financial Instruments*, which requires measurement and recognition of expected credit losses for financial assets by requiring an allowance to be recorded as an offset to the amortized cost of such assets. For available-for-sale debt securities, expected credit losses should be estimated when the fair value of the debt securities is below their associated amortized costs. This amendment is effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2019. Early adoption is permitted. The modified retrospective approach should be applied upon adoption of this new guidance. The Company has evaluated this amendment and it is not expected to have a material impact to the Company's financial statements.

3. Collaboration and License Revenue

The Company has not recorded revenues in the year ended December 31, 2019, and all revenues in the years ended December 31, 2018 and 2017, respectively, relate to an exclusive License and Collaboration Agreement (Collaboration Agreement) with Aventis Inc., a wholly-owned subsidiary of Sanofi. The Collaboration Agreement provided for the research, development and potential commercialization of pharmaceutical products for the treatment, prevention and diagnosis of hypertrophic and dilated cardiomyopathy, as well as potential additional indications. Revenues for the two years ended December 31, 2018 and 2017, respectively, relate to a $45.0 million payment received from Sanofi in January 2017 as a non-refundable continuation payment for such research and development. The $45.0 million was recognized pro-rata over the two-year period ending December 31, 2018 based on a cost-based input method and was recorded proportionally in relation to the Company's research and development effort over those periods.

The Collaboration Agreement provided for a termination clause whereby on or before December 31, 2018, Sanofi was required to notify the Company of its intent to continue the collaboration and on December 31, 2018 Sanofi notified the Company it was not continuing the collaboration; however, certain royalty rights remained with Sanofi. In July 2019, the Company and Sanofi entered into a Termination Agreement and the Company reacquired these U.S. royalty rights for $80.0 million, of which $50.0 million was paid immediately and $30.0 million was deposited into escrow to be paid to Sanofi by June 30, 2020 without conditions. The Company also paid $4.3 million to Sanofi for certain of its assets related to the danicamtiv program. Neither the Company nor Sanofi have further obligations under the Collaboration Agreement that would prevent the payment of the escrowed amount. As a result of the Termination Agreement, there are no further rights or obligations between the parties.

Revenue Recognition in 2018 and 2017

The Company implemented ASC 606 using the full retrospective transition method effective January 1, 2018 and revised its revenue for the years ended December 31, 2016 and 2017 accordingly. The Company evaluated the Collaboration Agreement under ASC 606 and determined that it had the following performance obligations to Sanofi:

1. the licenses of intellectual property for each of the HCM-1, HCM-2 and DCM-1 compound development programs, and

2. the performance of research and development services, including regulatory support, for each of the three programs.

The Company considered whether the licenses had standalone functionality and were capable of being distinct; however, given the fact that the research and development services were of such a specialized nature that could only be performed by the Company and Sanofi could not benefit from the intellectual property licenses without the Company's performance, the Company determined that the intellectual property licenses were not distinct from the research and development services and thus the license and research and development services for each program were combined into three separate performance obligations.

Contract Term

For revenue recognition purposes, the Company determined that the Collaboration Agreement was a period to period contract for which the Company had enforceable rights and obligations from inception through the initial term of December 31, 2016. Sanofi had the right to terminate the Collaboration Agreement prior to December 31, 2016 or to extend the contract term through December 31, 2018. If Sanofi had elected to terminate the agreement, the termination would have taken effect on December 31, 2016 and all licensed rights would have reverted to the Company. The Company did not have any obligation to reimburse Sanofi any portion of the payments received if Sanofi had terminated the agreement.

In December 2016, Sanofi elected to continue the Collaboration Agreement for an extended term ending December 31, 2018 and made a $45.0 million continuation payment to the Company in January 2017. The Company determined that the extended term was to be treated as a separate contract because such an extension was not probable at the inception of the contract, the extension represented additional goods and services, and such activities were priced commensurate to the effort required and did not involve any significant discount. It was also concluded that the extended term provided the Company with enforceable rights and obligations for the two-year period ended December 31, 2018. Because Sanofi retained the option in the Collaboration Agreement to extend the arrangement, neither party was committed to perform and the contract did not have enforceable rights and obligations beyond December 31, 2018.

Transaction Price

The Company's assessment of the transaction price included an analysis of amounts to which it was expected to be entitled for providing goods or services to the customer. The extended term (from January 1, 2017 to December 31, 2018) had a fixed fee of $45.0 million, paid by Sanofi contemporaneously with the notice of continuation of the contract. The Company therefore determined that the transaction price for this extended term was $45.0 million and this amount was recognized over the periods ending December 31, 2018 and 2017, respectively.

As noted above, the Collaboration Agreement included up to $45.0 million in funding from Sanofi of approved in-kind research and clinical activities. Sanofi was the decision maker on how to provide these services and such services were used in the development of joint program technology which is co-owned by both parties. As such the Company concluded that these in-kind contributions did not constitute consideration paid by Sanofi to the Company.

Any consideration related to sales-based royalties were to be recognized when the related sales occurred and therefore have also been excluded from the transaction price.

Methodology for Recognition

Since the Company determined that the three performance obligations were satisfied over time, the Company selected a single revenue recognition method that it believed most faithfully depicts the Company's performance in transferring control of the services. ASC 606 allows entities to choose between two methods to measure progress toward complete satisfaction of a performance obligation:

1. Output methods - recognize revenue on the basis of direct measurements of the value to the customer of the goods or services transferred to date relative to the remaining goods or services promised under the contract (e.g. surveys of performance completed to date, appraisals of results achieved, milestones reached, time elapsed, and units produced, or units delivered); or

2. Input methods - recognize revenue on the basis of the entity's efforts or inputs to the satisfaction of a performance obligation (e.g., resources consumed, labor hours expended, costs incurred, or time elapsed) relative to the total expected inputs to the satisfaction of that performance obligation.

The Company utilized a cost-based input method to measure proportional performance and calculated the corresponding amount of revenue to recognize. The Company believed this was the best measure of progress because other measures did not reflect how the Company executed its performance obligations under the contract with Sanofi. In applying the cost-based input methods of revenue recognition, the Company used actual costs incurred relative to budgeted costs to fulfill the combined performance obligations. Revenue was recognized based on actual costs incurred as a percentage of total actual and budgeted costs as the Company completed its performance obligations, which were fulfilled on December 31, 2018. A cost-based input method of revenue recognition requires management to make estimates of costs to complete the Company's performance obligations. In making such estimates, significant judgment is required to evaluate assumptions related to cost estimates. The cumulative effect of revisions to estimated costs to complete the Company's performance obligations were recorded in the period in which changes were identified and amounts could be reasonably estimated.

For the years ended December 31, 2019, 2018 and 2017, the Company recognized zero, $33.6 million and, $11.4 million of collaboration and license revenue, respectively. The Company will not recognize any further revenue from the Collaboration Agreement.

There were no contract assets or liabilities during the year ended December 31, 2019. The following table presents changes in the Company's contract assets and liabilities, which excludes research and development reimbursements under the cost sharing plan further discussed below, for the year ended December 31, 2018 (in thousands):

	Year Ended December 31, 2018			
	Balance at Beginning of Period	Additions	Deductions	Balance at End of Period
Contract liabilities:				
Deferred revenue	$ 33,558	$ —	$ (33,558)	$ —

Cost Sharing

During the years ended December 31, 2019, 2018 and 2017, the Company received research and development cost reimbursements from Sanofi under the terms of the Collaboration Agreement.

Since the inception of the Collaboration Agreement and up until December 31, 2018, Sanofi had been conditionally responsible for reimbursing the Company for:

(i) one half or more of the registration program plan (RPP) costs after clinical proof-of-concept had been established for the lead compound under each of the HCM-1 and HCM-2 programs; and

(ii) if the Company had initiated a clinical trial of a compound under a proof-of-concept development plan and not terminated its development thereof and if an additional compound had been identified as a development candidate for the same program, the Company was entitled to full reimbursement of pre-proof-of-concept (pre-POC)

(iii) research and development costs on development candidates mutually identified as such additional compounds, with the objective of conducting IND-enabling studies and clinical trials on such candidate.

Effective October 2017, and through June 30, 2019, Sanofi shared RPP costs for the mavacamten program pursuant to the Collaboration Agreement termination terms. Registration program costs approved by the Company and Sanofi included amounts incurred relating to clinical trials, development and manufacturing of, and obtaining regulatory approvals for mavacamten, and included direct employee costs and direct out-of-pocket costs incurred, by or on behalf of a party, specifically identifiable or reasonably and directly allocable to those activities.

Pursuant to the additional compounds provisions of the Collaboration Agreement, in August 2018 Sanofi agreed to reimburse the Company for eligible costs it incurred in the development of the MYK-224 compound, which had been identified as an additional compound under the HCM-1 program. Eligible costs were subject to review and approval under the same procedures as under the RPP program; reimbursable costs consisted of research and development activities agreed to by the Company and Sanofi that were negotiated and budgeted prior to the application for reimbursement. Reimbursements for this compound continued through March 31, 2019, in accordance to the Collaboration Agreement termination terms.

Estimated reimbursements were invoiced to Sanofi before each interim period based on budgeted amounts. For the RPP program, these estimates consisted of one half of the Company's mavacamten development budget in excess of Sanofi's mavacamten development budget each interim period and the entire MYK-224 budget which was reimbursable in full. Actual amounts received from Sanofi were applied to the applicable interim period to reduce the Company's research and development expenses.

Due to the termination of the license agreement effective December 31, 2018, the Company has not received reimbursements for the MYK-224 compound for any periods subsequent to April 1, 2019 and for the mavacamten compound subsequent to July 1, 2019.

The Company recorded $18.5 million, $23.1 million and $7.3 million as reductions to research and development expenses for the years ended December 31, 2019, 2018 and 2017, respectively. The following table presents the Sanofi prepayments and reimbursed research and development expenses for the years ended December 31, 2019, 2018 and 2017 (in thousands):

	Year Ended December 31,		
	2019	2018	2017
Balance at beginning of year	$ 12,973	$ 4,432	$ —
Additions for advance billings	—	—	1,013
Payments received from Sanofi	5,521	31,659	10,697
Actual expenses incurred	(18,494)	(23,118)	(7,278)
Balance at end of year	$ —	$ 12,973	$ 4,432

4. Fair Value Measurements

Fair value accounting is applied for all financial assets and liabilities, including short-term and long-term investments, and non-financial assets and liabilities that are recognized or disclosed at fair value in the consolidated financial statements on a recurring basis (at least annually). The carrying amount of the Company's financial instruments, including accounts payable and accrued liabilities and other current liabilities approximate fair value due to their short-term maturities.

Marketable securities are stated at their estimated fair values. The counterparties to the agreements relating to the Company's investment securities consist of the U.S. Treasury, governmental agencies, various major corporations and financial institutions with high credit standing. The carrying amounts for financial instruments consisting of cash and cash equivalents, receivable from collaboration partner, accounts payable and accrued liabilities approximate fair value due to their short maturities.

The accounting guidance for fair value provides a framework for measuring fair value, clarifies the definition of fair value and expands disclosures regarding fair value measurements. Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability (an exit price) in an orderly transaction between market participants at the reporting date. The accounting guidance establishes a three-tiered hierarchy, which prioritizes the inputs used in the valuation methodologies in measuring fair value as follows:

Level 1—Inputs are unadjusted, quoted prices in active markets for identical assets or liabilities at the measurement date.

Level 2—Inputs other than quoted market prices included in Level 1 are either directly or indirectly observable for the asset or liability through correlation with market data at the measurement date and for the duration of the instrument's anticipated life.

Level 3—Inputs reflect management's best estimate of what market participants would use in pricing the asset or liability at the measurement date. Consideration is given to the risk inherent in the valuation technique and the risk inherent in the inputs to the model.

All investments have been classified as "available-for-sale" and are carried at fair value based upon quoted market prices or pricing models for similar securities at period end. Generally, those investments with contractual maturities greater than 12 months are considered long-term investments. Unrealized gains and losses, deemed temporary in nature, are reported as a component of accumulated other comprehensive loss, net of tax, on the consolidated balance sheets.

A decline in the fair value of any security below cost that is deemed other than temporary results in a charge to earnings and the corresponding establishment of a new cost basis for the security. The amortized cost of securities is adjusted for amortization of premiums and accretion of discounts to maturity. Dividend and interest income are recognized when earned. Realized gains and losses are included in earnings and are derived using the specific identification method for determining the cost of securities sold.

The following table sets forth the Company's financial instruments that were measured at fair value on a recurring basis by level within the fair value hierarchy (in thousands):

	Fair Value Measurements at December 31, 2019			
	Total	Level 1	Level 2	Level 3
Assets				
Money market funds	$ 100,441	$ 100,441	$ —	$ —
U.S. government agency obligations	134,055	—	134,055	—
Corporate securities	194,789	—	194,789	—
Total	$ 429,285	$ 100,441	$ 328,844	$ —

	Fair Value Measurements at December 31, 2018			
	Total	Level 1	Level 2	Level 3
Assets				
Money market funds	$ 245,194	$ 245,194	$ —	$ —
U.S. government agency obligations	85,033	—	85,033	—
Corporate securities	63,679	—	63,679	—
Total	$ 393,906	$ 245,194	$ 148,712	$ —

The following table is a summary of amortized cost, unrealized gain and loss, and fair value (in thousands) of the Company's marketable securities by contractual maturities:

	Fair Value Measurements at December 31, 2019			
	Amortized Cost	Unrealized Gain	Unrealized Loss	Fair Value
Cash equivalents (due within 90 days)	$ 100,440	$ 1	$ —	$ 100,441
Short-term investments (due within one year)	314,181	523	(13)	314,691
Long-term investments (due between one and two years)	14,110	47	(4)	14,153
Total	$ 428,731	$ 571	$ (17)	$ 429,285

	Fair Value Measurements at December 31, 2018			
	Amortized Cost	Unrealized Gain	Unrealized Loss	Fair Value
Cash equivalents (due within 90 days)	$ 245,194	$ —	$ —	$ 245,194
Short-term investments (due within one year)	68,656	—	(92)	68,564
Long-term investments (due between one and two years)	80,118	98	(68)	80,148
Total	$ 393,968	$ 98	$ (160)	$ 393,906

The Company recognizes transfers between levels of the fair value hierarchy as of the end of the reporting period. There were no transfers within the hierarchy during the years ended December 31, 2019 and 2018. There were no material realized gains or losses on available-for- sale securities during the periods presented.

5. Balance Sheet Components

Property and Equipment

Property and equipment are stated at cost and depreciated using the straight-line method over the estimated useful lives of the assets, ranging from two to five years. Leasehold improvements are amortized over the shorter of their estimated useful lives or the related lease term. Upon retirement or sale, the cost and related accumulated depreciation are removed from the consolidated balance sheet and the resulting gain or loss is reflected in the consolidated statement of operations and comprehensive loss.

Property and equipment consists of the following (in thousands):

	December 31,	
	2019	2018
Scientific equipment	$ 10,642	$ 9,126
Furniture and equipment	2,572	1,248
Capitalized software	389	302
Leasehold improvements	509	451
Construction in progress	9,568	—
Total	23,680	11,127
Less: Accumulated depreciation	(7,937)	(5,989)
Property and equipment, net	$ 15,743	$ 5,138

Depreciation expense was $1.9 million, $1.6 million and $1.3 million for the years ended December 31, 2019, 2018 and 2017, respectively. Construction in progress consists of leasehold improvements made to the Company's Brisbane, California facility in preparation for occupancy in January 2020.

The Company reviews long-lived assets, including property and equipment, for impairment whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. An impairment charge would be recorded when estimated undiscounted future cash flows expected to result from the use of the asset and its eventual disposition are less than its carrying amount. Impairment, if any, is assessed using discounted cash flows or other appropriate measures of fair value. Through December 31, 2019, there have been no such impairment charges.

Accrued Liabilities

Accrued liabilities consist of the following (in thousands):

	December 31,	
	2019	2018
Clinical trials accrued liabilities	$ 11,494	$ 6,272
Outside services	6,592	4,631
Payroll-related liabilities	11,724	8,151
Construction in progress	9,139	—
Other	2,343	1,704
Total accrued liabilities	$ 41,292	$ 20,758

Construction in progress consists of leasehold improvements made to the Company's Brisbane, California facility in preparation for occupancy in January 2020.

6. Leases

The Company determines if an arrangement is or contains a lease at inception. Operating lease right-of-use (ROU) assets and liabilities are presented separately on our consolidated balance sheets. The Company does not have any finance leases.

Operating lease ROU assets and operating lease liabilities are recognized based on the present value of the future minimum lease payments over the lease term beginning at the commencement date. As the Company's leases do not provide enough information to determine an implicit interest rate, the Company determines its incremental borrowing rate based on the rate of interest that the Company would have to pay to borrow on a collateralized basis over a similar term in a similar economic environment. The operating lease ROU assets also include any lease payments made and excludes lease incentives and initial direct costs incurred. Lease terms may include options to extend or terminate the lease when it is reasonably certain that the Company will exercise that option. Lease expense for minimum lease payments is recognized on a straight-line basis over the lease term.

As of December 31, 2019, the Company has operating leases for approximately 56,500 square feet of office and lab space in two separate facilities in South San Francisco, California (the "Existing Facilities"). All of the lease agreements associated with the Existing Facilities expire on or before April 30, 2020 and there are no options to extend the leases. The Company does not plan to cancel the existing lease agreements for its Existing Facilities prior to their respective expiration dates.

Information related to operating leases as of December 31, 2019 and upon adoption of ASC 842 on January 1, 2019 is as follows (in thousands, except for percentages and years):

	December 31, 2019	January 1, 2019
Assets		
Operating lease right-of-use assets	$ 417	$ 1,940
Liabilities		
Operating lease liabilities - current	$ 383	$ 2,126
Weighted average remaining lease term (years)	0.3	1.0
Weighted average discount rate	6%	6%

Information related to operating lease activity during the year ended December 31, 2019 follows (in thousands):

	Year Ended December 31, 2019
Operating lease right-of-use assets obtained in exchange for lease obligations	$ 1,095
Operating lease rental expense	$ 2,760
Operating lease payments	$ 3,007

Future annual payments of operating lease liabilities as of December 31, 2019 are as follows (in thousands):

Year ending December 31:	Amount
2020	387
Total future lease payments	387
Less: imputed interest	(4)
Total operating lease liabilities	$ 383

In September 2018, the Company entered into a noncancelable operating lease (the “Lease”) for approximately 129,800 square feet of space in Brisbane, California (the “New Facility”). As of December 31, 2019, the Company has capitalized $9.1 million of tenant improvements as construction in progress within property and equipment. The lease commencement date was in January 2020 and the Company will record the ROU asset and lease liability on its balance sheet in accordance with ASC 842 in the first quarter of 2020. The Company will also reclass the amount included as tenant improvement within property and equipment on the December 31, 2019 balance sheet to leasehold improvements within property and equipment and amortize it over the lease term of 10 years. The Lease grants the Company an option to extend the Lease for an additional 10-year period. As of December 31, 2019, future minimum rental payments under the Lease during the 10-year term are $93.2 million in the aggregate. The Lease further provides that the Company is obligated to pay to the landlord certain costs, including taxes and operating expenses.

In September 2018, the Company provided a standby letter of credit of $1.9 million as security for its obligations under the Lease. This standby letter of credit is classified on the balance sheet as restricted cash and other.

Future annual minimum operating lease payments due under the Lease are as follows (in thousands):

Year ending December 31:	Amount
2020	5,454
2021	8,461
2022	8,757
2023	9,063
2024	9,381
Thereafter	52,063
Total	$ 93,179

The adoption of ASC 842 did not materially affect the amount or timing of operating lease rent expense to be recognized during the year ended December 31, 2019 as compared to accounting under the prior guidance. Operating lease rent expense for the year ended December 31, 2019, 2018 and 2017 was $2.8 million, $2.1 million and $1.4 million, respectively, which is included in operating expenses on the Company’s consolidated statements of operations and comprehensive loss. The operating leases require the Company to share in prorated operating expenses and property taxes based upon actual amounts incurred; those amounts are not fixed for future periods and, therefore, are not included in the future commitments listed above.

7. Commitments and Contingencies

Purchase Commitments

The Company conducts product research and development programs through a combination of internal and collaborative programs that include, among others, arrangements with universities, contract research organizations and clinical research sites. The Company has contractual arrangements with these organizations; however, these contracts are generally cancelable on 30 days' notice and the obligations under these contracts are largely based on services performed.

Contingencies

From time to time, the Company may have contingent liabilities that arise in the ordinary course of business activities. The Company accrues for such a liability when it is probable that future expenditures will be made, and such expenditures can be reasonably estimated. There were no contingent liabilities requiring accrual or disclosure as of December 31, 2019 and 2018.

Guarantees and Indemnifications

The Company enters into standard indemnification arrangements in the ordinary course of business. Pursuant to certain of these arrangements, the Company indemnifies, holds harmless, and agrees to reimburse the indemnified parties for losses suffered or incurred by the indemnified party, in connection with any trade secret, copyright, patent or other intellectual property infringement claim by any third-party with respect to the Company's technology. The term of these indemnification arrangements is generally perpetual. The maximum potential amount of future payments the Company could be required to make under these agreements is not determinable because it involves claims that may be made against the Company in the future but have not yet been made.

The Company indemnifies its officers and directors for certain events or occurrences, subject to certain limits, while the officer or director is or was serving at the Company's request in such capacity, as permitted under Delaware law and in accordance with its certificate of incorporation and bylaws, and agreements providing for indemnification entered into with its officers and directors. The term of the indemnification period lasts as long as an officer or director may be subject to any proceeding arising out of acts or omissions of such officer or director in such capacity.

The maximum amount of potential future indemnification of directors and officers is unlimited; however, the Company currently holds director and officer liability insurance. This insurance allows the transfer of risk associated with its exposure and may enable it to recover a portion of any future amounts paid.

The Company believes that the fair value of these indemnification obligations is minimal. Accordingly, the Company has not recognized any liabilities relating to these obligations for any period presented.

8. Stockholders' Equity

On March 8, 2018, the Company filed a Registration Statement on Form S-3ASR (the "2018 Shelf Registration Statement") covering the potential offering, issuance, and sale of an indeterminate amount of common stock, preferred stock, debt securities, warrants and/or units. In March 2019, the Company completed a follow-on offering under the 2018 Shelf Registration Statement in which the Company issued 5,663,750 shares of common stock at a price of $51.00 per share, including 738,750 shares sold directly to the underwriters upon exercise of their option to purchase up to 738,750 shares of the Company's common stock within 30 days of the offering. During the year ended December 31, 2019, the Company received proceeds totaling approximately $271.2 million from the offering, net of underwriting discounts and commissions and offering expenses.

Common Stock Reserved for Issuance

The Company has reserved shares of common stock, on an as-if-converted basis, for issuance as follows:

	December 31, 2019	December 31, 2018
Options and awards issued and outstanding	5,315,254	3,864,407
Shares available for issuance under 2015 Stock Option and Incentive Plan	685,435	904,785
Shares available for issuance under 2015 Employee Stock Purchase Plan	1,140,541	780,716
Total	7,141,230	5,549,908

Preferred stock

As amended in November 2015, the Company's Certificate of Incorporation authorizes 5,000,000 shares of preferred stock at a par value of $0.0001 per share. As of December 31, 2019, and 2018, no preferred stock was issued or outstanding.

9. Stock-Based Compensation

In June 2012, the Company adopted the 2012 Equity Incentive Plan (as amended, the 2012 Plan). The 2012 Plan provides for the granting of incentive stock options, nonstatutory stock options, restricted stock units (RSUs), stock bonuses and rights to acquire restricted stock to employees, officers, directors and consultants. Incentive stock options may be granted with exercise prices of not less than 100% of the estimated fair value of the common stock and nonstatutory stock options may be granted with an exercise price of not less than 85% of the estimated fair value of the common stock on the date of grant. Stock options granted to a stockholder owning more than 10% of the voting stock must have an exercise price of not less than 110% of the estimated fair value of the common stock on the date of grant. The Board of Directors determines the estimated fair value of common stock. Stock options were generally granted with terms of up to ten years and vest over a period of four years. Upon the exercise of options, the Company issues new common stock from its authorized shares. Effective with the Company's initial public offering in August 2015, the Company no longer issues shares from this plan and all cancelled or forfeited shares are returned to the 2015 Stock Option and Incentive Plan.

In October 2015, the Company's Board of Directors and stockholders adopted the 2015 Stock Option and Incentive Plan (the 2015 Plan) and the 2015 Employee Stock Purchase Plan (2015 ESPP). Under the 2015 Plan, 1,650,000 shares of common stock were initially reserved for issuance, as of the pricing of the Company's initial public offering. The number of shares initially reserved for issuance under the 2015 Plan will be increased by (i) the number of shares represented by awards outstanding under the Company's 2012 Equity Incentive Plan that are forfeited or lapse unexercised and which following the pricing date are not issued under the 2012 Plan, and (ii) an annual increase on January 1 of each year beginning on January 1, 2017. Effective January 1, 2020 and 2019, the Company reserved an additional 1,855,162 and 1,611,557 shares of common stock, respectively, for issuance under the 2015 Plan.

The Company began issuing RSUs to employees under the 2015 Plan during the year ended December 31, 2018. RSUs settle into shares of common stock upon vesting, generally over a four-year period, and the fair value is the market price on the date of grant. During the year ended December 31, 2019, the Company also granted certain key employees performance-based RSUs.

The Company accounts for stock-based compensation arrangements with employees in accordance with ASC 718, *Stock Compensation.* Stock-based awards granted include stock options with time-based vesting, performance-based stock options, and restricted stock units (RSUs). ASC 718 requires the recognition of compensation expense, using a fair value-based method, for costs related to all stock-based payments. The Company's determination of the fair value of stock options with time-based vesting on the date of grant utilizes the Black-Scholes option-pricing model, and is impacted by its common stock price as well as other variables including, but not limited to, expected term that options will remain outstanding, expected common stock price volatility over the term of the option awards, risk-free interest rates and expected dividends.

Stock-based compensation expense for performance stock options and RSUs is based on the probability of achieving certain performance criteria, as defined in the individual grant agreement. The Company estimates the number of performance options and RSUs ultimately expected to vest and recognizes stock-based compensation expense for those options and RSUs expected to vest when it becomes probable that the performance criteria will be met.

The fair value of a stock-based award is recognized over the period during which a grantee is required to provide services in exchange for the option or RSU award, known as the requisite service period (usually the vesting period), on a straight-line basis. The Company accounts for forfeitures as they occur.

Equity instruments issued to non-employees are recorded at their fair value on the grant date. The fair value of options granted to consultants is expensed over the non-employees' vesting period. Non-employee stock-based compensation expense was not material for all periods presented.

Estimating the fair value of equity-settled awards as of the grant date using valuation models, such as the Black-Scholes option pricing model, is affected by assumptions regarding a number of complex variables. Changes in the assumptions can materially affect the fair value and ultimately how much stock-based compensation expense is recognized. These inputs are subjective and generally require significant analysis and judgment to develop.

Expected Term—The expected term assumption represents the weighted-average period that the Company's stock-based awards are expected to be outstanding. The expected term of the Company's options exceeds the number of years the Company has been a publicly held corporation; therefore, the Company has opted to use the "simplified method" for estimating the expected term of the options. The simplified method is calculated as average of the vesting term and the original contractual term of the option.

Expected Volatility—For all stock options granted to date, the volatility data was estimated based on a study of the Company's trading history and that of its publicly traded industry peer companies. For purposes of identifying these peer companies, the Company considered the industry, stage of development, size and financial leverage of potential comparable companies.

Expected Dividend—The Black-Scholes valuation model calls for a single expected dividend yield as an input. The Company currently has no history or expectation of paying cash dividends on its common stock.

Risk-Free Interest Rate—The risk-free interest rate is based on the yield available on U.S. Treasury zero-coupon issues similar in duration to the expected term of the equity-settled award.

In October 2015, the Company adopted the 2015 ESPP, which provides eligible employees with the opportunity to acquire an ownership interest in the Company through periodic payroll deductions, based on a six-month look-back period, at a price equal to the lesser of 85% of the fair market value of the common stock at either the first business day or last business day of the relevant offering period, provided that no more than 2,500 shares of common stock may be purchased by any one employee during each offering period. The 2015 ESPP is intended to constitute an "employee stock purchase plan" under Section 423(b) of the Internal Revenue Code of 1986, as amended. The 2015 ESPP may be terminated by the Company's board of directors at any time. A total of 255,000 shares of common stock were initially reserved for issuance under the 2015 ESPP, subject to an annual increase on January 1 of each year beginning on January 1, 2017. Effective January 1, 2020 and 2019, the Company reserved an additional 463,790 and 402,889 shares of common stock, respectively, for issuance under the 2015 ESPP.

Options

The following table summarizes stock option activity and related information for the periods presented below:

	Shares Subject to Outstanding Options	Weighted Average Exercise Price Per Option	Weighted Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Balance at December 31, 2018	3,701,461	$ 26.40		
Options granted	1,371,130	43.27		
Options exercised	(337,846)	15.78		
Options canceled	(160,587)	38.75		
Balance at December 31, 2019	4,574,158	$ 31.81	7.7	$ 187,879
Exercisable at December 31, 2019	2,380,560	$ 23.21	7.0	$ 118,246
Vested and expected to vest at December 31, 2019	4,574,158	$ 31.81	7.7	$ 187,879

The aggregate intrinsic value of options was calculated as the difference between the exercise price of the options and the estimated fair value of common stock. The aggregate intrinsic value of options exercised was $14.3 million, $21.1 million and $9.8 million for the years ended December 31, 2019, 2018 and 2017, respectively. The weighted-average grant date fair value of options granted under the Company's stock plans in the years ended December 31, 2019, 2018 and 2017 was $27.02, $34.70 and $9.92 per share, respectively. As of December 31, 2019, total unamortized stock-based compensation relating to options was $55.3 million, which is expected to be recognized over the average remaining vesting period of 2.4 years. The following table illustrates the assumptions for the Black-Scholes option-pricing model used in determining the fair value of time-based and performance-based options granted to employees:

	Year Ended December 31,		
	2019	2018	2017
Risk-free interest rate	1.59% - 2.54%	2.54% - 2.98%	1.92% - 2.27%
Expected life (in years)	6.1%	5.3 - 6.1	5.3 - 6.1
Volatility	65% - 69%	69% - 75%	71% - 75%
Dividend yield	0%	0%	0%

Restricted Stock Units

The following table summarizes RSU activity and related information for the period presented below:

	Shares Subject to Outstanding Awards	Weighted Average Grant Date Fair Value	Weighted Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Balance at December 31, 2018	162,946	$ 53.37		
RSUs awarded	643,814	45.36		
RSUs released	(42,214)	53.08		
RSUs forfeited	(23,450)	48.23		
Balance at December 31, 2019	741,096	$ 46.59	2.2	$ 54,015

The weighted -average grant-date fair value of RSUs granted during the years ended December 31, 2019 and 2018 was $45.36 and $53.27, respectively. The total fair value of RSUs vested during the years ended December 31, 2019, 2018 and 2017 was $2.0 million, $167,000 and zero, respectively. As of December 31, 2019, total unamortized stock-based compensation relating to RSUs was $27.9 million, which is expected to be recognized over the average remaining vesting period of 3.1 years.

Stock-Based Compensation

Stock-based compensation expense, net of forfeitures, as applicable for the years ended December 31, 2019, 2018 and 2017, is reflected in the statements of operations and comprehensive loss as follows (in thousands):

	Year Ended December 31,		
	2019	2018	2017
Research and development	$ 14,673	$ 8,144	$ 2,752
Selling, general and administrative	$ 18,321	11,197	3,386
Total stock-based compensation	$ 32,994	$ 19,341	$ 6,138

During the years ended December 31, 2018, 2017, and 2016, the Company recognized $340,000, $248,000 and $174,000 in stock-based compensation expense relating to stock options issued with performance-based vesting criteria, including the achievement of certain clinical and regulatory development milestones related to product candidates as well as commercial milestones. Recognition of stock-based compensation expense associated with these performance-based stock options commences when the performance condition is considered probable of achievement, using management's best estimates, which consider the inherent risk and uncertainty regarding the future outcomes of the activities described by the milestones.

10. Net Loss per Share

The following table sets forth the computation of basic and diluted net loss per share (in thousands, except share and per share data):

	Year Ended December 31,		
	2019	2018	2017
Numerator			
Net loss	$ (276,213)	$ (67,698)	$ (57,010)
Denominator			
Weighted average shares outstanding	44,767,581	38,466,233	33,098,571
Less: weighted average shares subject to repurchase	(2,085)	(79,327)	(266,057)
Weighted average shares used to compute basic and diluted net loss per share	44,765,496	38,386,906	32,832,514
Net loss per share, basic and diluted	$ (6.17)	$ (1.76)	$ (1.74)

Basic net loss per share is computed by dividing the net loss by the weighted average number of common shares outstanding for the period. Diluted net loss per share is computed by dividing the net loss by the weighted average number of common shares and potentially dilutive securities for the period, determined using the treasury-stock method and the as-if converted method, for convertible securities, if inclusion of these is dilutive. Because the Company has reported a net loss for all periods presented, diluted net loss per common share is the same as basic net loss per common share for those periods.

The following outstanding shares of potentially dilutive securities were excluded from the computation of diluted net loss per share for the periods presented because including them would have been antidilutive:

	As of December 31,		
	2019	2018	2017
Common stock subject to repurchase	—	9,790	81,373
Options and awards issued and outstanding	5,315,254	3,864,407	2,964,549

As of December 31, 2019, the Company has contributions from plan participants of $0.4 million under the 2015 ESPP, which if converted, would be equivalent to 10,000 shares based on 85% of the stock price at the beginning of the offering period. As of December 31, 2018, the Company had contributions from plan participants of $0.3 million under the 2015 ESPP, which if converted, would be equivalent to 5,700 shares based on 85% of the stock price at the beginning of the offering period.

11. Employee Benefit Plan

The Company sponsors a 401(k) Plan, which stipulates that eligible employees can elect to contribute to the 401(k) Plan, subject to certain limitations of eligible compensation.

12. Income Taxes

The Company accounts for income taxes under the asset and liability method. Current income tax expense or benefit represents the amount of income taxes expected to be payable or refundable for the current year. Deferred income tax assets and liabilities are determined based on differences between the financial statement reporting and tax bases of assets and liabilities and net operating loss and credit carryforwards and are measured using the enacted tax rates and laws that will be in effect when such items are expected to reverse. Deferred income tax assets are reduced, as necessary, by a valuation allowance when management determines it is more likely than not that some or all of the tax benefits will not be realized.

For each of the years ended December 31, 2019, 2018 and 2017, the effective income tax rate and tax provision from continuing operations was 0% for all periods, primarily attributable to losses generated and on which any income tax benefits are not likely to be realized.

The following is the reconciliation between the statutory federal income tax rate and the Company's effective tax rate:

	Year Ended December 31,		
	2019	2018	2017
Federal statutory income tax rate	21.0%	21.0%	34.0%
State taxes (tax effected)	7.3	8.6	7.1
Non-deductible expenses and other	(0.5)	2.5	2.0
Research and development reimbursements	3.2	5.9	6.0
Change in valuation allowance	(31.0)	(38.0)	(24.0)
Tax Act – net deferred tax rate change	—	—	(25.1)
Total	—%	—%	—%

As of December 31, 2019 and 2018, the components of the Company's deferred tax assets are as follows (in thousands):

	As of December 31,	
	2019	2018
Deferred tax assets:		
Net operating loss carryforwards	98,445	49,689
Research and development reimbursement carryforwards	23,061	12,908
Stock-based compensation	8,861	4,349
Start-up costs	22,896	1,237
Depreciation	(1,027)	(959)
Other	2,646	1,858
Total deferred tax assets	154,882	69,082
Less: valuation allowance	(154,882)	(69,082)
Net deferred tax assets	—	—

The Company's primary deferred tax assets of $98.4 million and $49.7 million at December 31, 2019 and 2018, respectively, relate to its net operating loss carryforwards (NOLs). Based on a history of cumulative losses in recent periods and consideration of other available positive and negative evidence, the Company has recorded a full valuation allowance to offset the deferred tax assets for both periods presented.

As of December 31, 2019, the Company had approximately $351.1 million and $354.0 million of federal and state net operating losses, respectively, that will begin to expire in 2032. As of December 31, 2019, the Company had approximately $7.2 million and $5.9 million of federal and state research and development tax credit carryovers, respectively. If not utilized, the federal credit carryforward will expire in 2032, and the state credit carryforward does not expire. As of December 31, 2019, the Company had approximately $18.2 million of federal orphan tax credit carryovers, which will begin to expire in 2036 if not utilized. The valuation allowance increased by approximately $85.8 million, $25.7 million and $13.7 million during the years ended December 31, 2019, 2018 and 2017, respectively.

Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (the Code) if a corporation undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership over a rolling three-year period, the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes (such as research tax credits) to offset its post-change income or taxes may be limited. Similar rules may apply under the laws of the state of California. The annual limitation generally is determined by multiplying the value of the Company's stock at the time of such ownership change (subject to certain adjustments) by the applicable "long-term tax-exempt rate." Such limitations may result in expiration of a portion of the NOLs and other tax attributes before utilization. Each ownership change resulted in an annual limitation, but all NOLs and other tax attributes generated prior to the ownership changes on April 20, 2015 and August 14, 2017 can be utilized prior to expiration if the Company earns sufficient taxable income. The Company's March 2019 follow-on stock offering did not result in an ownership change.

As of December 31, 2019, and 2018, the Company did not have a liability related to unrecognized tax benefits. All unrecognized tax benefits have been netted against the research and development and orphan drug credit carryforwards deferred tax asset.

The Company records interest and penalties related to unrecognized tax benefits within interest and other income, net. As of December 31, 2019, and 2018, the Company had not accrued any interest or penalties related to unrecognized tax benefits. The Company is subject to U.S. federal and California income tax assessment for years beginning in 2012 and Australia beginning in 2015. However, since the Company has incurred federal and California net operating losses every year since inception, all of its income tax returns are subject to examination and adjustments by the Internal Revenue Service for at least three years and by the California Franchise Tax Board for four years following the year in which the tax attributes are utilized. The Company does not

believe that there will be a material change in its unrecognized tax positions over the next twelve months. There is no amount of unrecognized tax benefit that, if recognized, would affect the effective tax rate.

Uncertain Tax Positions

The Company accounts for uncertain tax positions in accordance with ASC 740-10, *Accounting for Uncertainty in Income Taxes.* The Company assesses all material positions taken in any income tax return, including all significant uncertain positions, in all tax years that are still subject to assessment or challenge by relevant taxing authorities. Assessing an uncertain tax position begins with the initial determination of the position's sustainability and is measured at the largest amount of benefit that is greater than 50% likely of being realized upon ultimate settlement. As of each balance sheet date, unresolved uncertain tax positions must be reassessed, and the Company determines whether (i) the factors underlying the sustainability assertion have changed and (ii) the amount of the recognized tax benefit is still appropriate. The recognition and measurement of tax benefits requires significant judgment. Judgments concerning the recognition and measurement of a tax benefit might change as new information becomes available.

The Company includes penalties and interest expense related to income taxes as a component of interest and other income, net; there were no interest or penalties accrued at December 31, 2019 and 2018.

The Company has not been audited by the Internal Revenue Service, any state tax authority, or foreign tax authorities. It is subject to taxation in the United States and Australia. Because of the net operating loss, research credit carryforwards, and orphan drug tax credit carryforwards, substantially all of its tax years, from 2012 to 2019, remain open to U.S. federal and California tax examinations. The statute of limitation in Australia is four years.

At December 31, 2019, 2018 and 2017, the Company's reserve for unrecognized tax benefits is approximately $7.5 million, $3.8 million and $2.5 million, respectively. Due to the full valuation allowance at December 31, 2019, current adjustments to the unrecognized benefits will have no impact to the Company's effective income tax rate.

A reconciliation of the beginning and ending amount of unrecognized tax benefits is as follows (in thousands):

	For the Year Ended December 31,		
	2019	2018	2017
Beginning balance	$ 3,810	$ 2,471	$ 1,474
Increases (decreases) of unrecognized tax benefits related to prior year	380	289	(97)
Increases of unrecognized tax benefits related to current year	3,314	1,050	1,094
Ending balance	$ 7,504	$ 3,810	$ 2,471

The Company does not anticipate material changes to its uncertain tax positions through the next twelve months.

13. Quarterly Financial Data (unaudited)

The following table summarizes the unaudited quarterly financial data for the last two fiscal years (in thousands, except per share data):

(in thousands, except share and per share amounts)	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
2019				
Revenues	$ —	$ —	$ —	$ —
Total operating expenses	$ 39,741	$ 41,564	$ 145,118	$ 61,411
Net loss	$ (37,470)	$ (38,174)	$ (141,802)	$ (58,767)
Net loss per common share, basic and diluted	$ (0.93)	$ (0.83)	$ (3.07)	$ (1.27)
Weighted average number of shares, basic and diluted	40,506,313	46,065,901	46,133,068	46,278,409
2018				
Revenues	$ 5,331	$ 6,639	$ 9,188	$ 12,400
Total operating expenses	$ 23,931	$ 26,130	$ 26,867	$ 30,281
Net loss	$ (17,820)	$ (18,413)	$ (15,789)	$ (15,676)
Net loss per common share, basic and diluted	$ (0.50)	$ (0.49)	$ (0.39)	$ (0.39)
Weighted average number of shares, basic and diluted	35,827,235	37,440,024	40,116,644	40,259,575

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

MYOKARDIA, INC.

February 27, 2020

By: /s/ T. Anastasios Gianakakos
T. Anastasios Gianakakos
Chief Executive Officer
(Principal Executive Officer and Authorized Signatory)

POWER OF ATTORNEY

KNOW ALL MEN BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints each of T. Anastasios Gianakakos and Taylor Harris, as his true and lawful attorney-in-fact and agent, with full power of substitution for him, and in his name in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, full power and authority to do and perform each and every act and thing requisite and necessary to be done therewith, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents and their respective substitute or substitutes, may lawfully do or cause to be done by virtue hereof. Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this report on Form 10-K has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ T. Anastasios Gianakakos T. Anastasios Gianakakos	President, Chief Executive Officer and Director (Principal Executive Officer)	February 27, 2020
/s/ Taylor Harris Taylor Harris	Chief Financial Officer (Principal Financial and Accounting Officer)	February 27, 2020
/s/ Sunil Agarwal Sunil Agarwal, M.D.	Director	February 27, 2020
/s/ Mary Cranston Mary B. Cranston	Director	February 27, 2020
/s/ David P. Meeker David P. Meeker, M.D.	Director	February 27, 2020
/s/ Mark L. Perry Mark L. Perry	Director	February 27, 2020
/s/ Kimberly Popovits Kimberly Popovits	Director	February 27, 2020
/s/ Wendy Yarno Wendy Yarno	Director	February 27, 2020

DESCRIPTION OF THE REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934

As of December 31, 2019, MyoKardia, Inc. (the "Company," "we," "us," and "our") had one class of securities registered under Section 12 of the Securities Exchange Act of 1934, as amended: our Common Stock.

Description of Common Stock

The following description of our Common Stock is a summary and does not purport to be complete. It is subject to and qualified in its entirety by reference to our Restated Certificate of Incorporation ("Certificate of Incorporation") and our Amended and Restated Bylaws ("Bylaws"), each of which are incorporated by reference as an exhibit to the Annual Report on Form 10-K of which this Exhibit 4.2 is a part, and by applicable law. We encourage you to read our Certificate of Incorporation, our Bylaws and the applicable provisions of the Delaware General Corporation Law for additional information.

Authorized Capital Stock

Our authorized capital stock consists of 150,000,000 shares of common stock, par value $0.0001 per share (the "Common Stock"), and 5,000,000 shares of preferred stock, par value $0.0001 per share (the "Preferred Stock"), all of which shares of Preferred Stock are undesignated.

Common Stock

The holders of our Common Stock are entitled to one vote for each share held on all matters submitted to a vote of the stockholders. The holders of our Common Stock do not have any cumulative voting rights. Holders of our Common Stock are entitled to receive ratably any dividends declared by our board of directors (the "Board") out of funds legally available for that purpose, subject to any preferential dividend rights of any outstanding Preferred Stock. Our Common Stock has no preemptive rights, conversion rights or other subscription rights or redemption or sinking fund provisions. In the event of our liquidation, dissolution or winding up, holders of our Common Stock will be entitled to share ratably in all assets remaining after payment of all debts and other liabilities and any liquidation preference of any outstanding Preferred Stock. All outstanding shares are fully paid and nonassessable.

Our Common Stock is listed on The Nasdaq Global Select Market under the symbol "MYOK."

The transfer agent and registrar for our Common Stock is Computershare Trust Company, N.A.

Preferred Stock - Limitations on Rights of Holders of Common Stock

Our Board is authorized to issue up to 5,000,000 shares of undesignated Preferred Stock in one or more series without stockholder approval. Our Board may determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of Preferred Stock. The purpose of authorizing our Board to issue Preferred Stock in one or more series and determine the number of shares in the series and its rights and preferences is to eliminate delays associated with a stockholder vote on specific issuances. Examples of rights and preferences that the Board may fix are: dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of such series, any or all of which may be greater than the rights of our Common Stock. The rights of holders of our Common Stock will be subject to, and may be adversely affected by, the rights of any Preferred Stock that we may designate and issue in the future. The issuance of shares of undesignated Preferred Stock could decrease the amount of earnings and assets available for distribution to holders of shares of Common Stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

Antitakeover Effects of Delaware Law and Provisions of our Certificate of Incorporation and Bylaws

Certain provisions of the Delaware General Corporation Law and of our Certificate of Incorporation and Bylaws could have the effect of delaying, deferring or discouraging another party from acquiring control of us. These provisions, which are summarized below, are expected to discourage certain types of coercive takeover practices and inadequate takeover bids and, as a consequence, they might also inhibit temporary fluctuations in the market price of our Common Stock that often result from actual or rumored hostile takeover attempts. These provisions are also designed in part to encourage anyone seeking to acquire control of us to first negotiate with our Board. These provisions might also have the effect of preventing changes in our management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders might otherwise deem to be in their best interests. However, we believe that the advantages gained by protecting our ability to negotiate with any unsolicited and potentially unfriendly acquirer outweigh the disadvantages of discouraging such proposals, including those priced above the then-current market value of our Common Stock, because, among other reasons, the negotiation of such proposals could improve their terms.

Delaware Takeover Statute

We are subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, our Board approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances, but not the outstanding voting stock owned by the interested stockholder; or
- at or after the time the stockholder became interested, the business combination was approved by our Board and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines a business combination to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, lease, pledge, exchange, mortgage or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;
- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- subject to exceptions, any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; or
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

Provisions of our Certificate of Incorporation and Bylaws

Our Certificate of Incorporation and Bylaws include a number of provisions that may have the effect of delaying, deferring or discouraging another party from acquiring control of us and encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our Board rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

Board composition and filling vacancies. In accordance with our Certificate of Incorporation, our Board is divided into three classes serving staggered three-year terms, with one class being elected each year. Our Certificate of Incorporation also provides that directors may be removed only for cause and then only by the affirmative vote of the holders of 75% or more of the shares then entitled to vote at an election of directors. Furthermore, any vacancy on our Board, however occurring, including a vacancy resulting from an increase in the size of our Board, may only be filled by the affirmative vote of a majority of our directors then in office even if less than a quorum.

No written consent of stockholders. Our Certificate of Incorporation provides that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting. This limit may lengthen the amount of time required to take stockholder actions and would prevent the amendment of our Bylaws or removal of directors by our stockholders without holding a meeting of stockholders.

Meetings of stockholders. Our Bylaws provide that only a majority of the members of our Board then in office may call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders. Our Bylaws limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

Advance notice requirements. Our Bylaws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days or more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. The notice must contain certain information specified in our Bylaws.

Amendment to Certificate of Incorporation and Bylaws. As required by the Delaware General Corporation Law, any amendment of our Certificate of Incorporation must first be approved by a majority of our Board, and if required by law or our Certificate of Incorporation, must thereafter be approved by a majority of the outstanding shares entitled to vote on the amendment, and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to stockholder action, directors, limitation of liability and the amendment of our Certificate of Incorporation must be approved by not less than 75% of the outstanding shares entitled to vote on the amendment, and not less than 75% of the outstanding shares of each class entitled to vote thereon as a class. Our Bylaws may be amended by the affirmative vote of a majority of the directors then in office, subject to any limitations set forth in the Bylaws; and may also be amended by the affirmative vote of at least 75% of the outstanding shares entitled to vote on the amendment, or, if the Board recommends that the stockholders approve the amendment, by the affirmative vote of the majority of the outstanding shares entitled to vote on the amendment, in each case voting together as a single class.

List of Subsidiaries of Registrant

MyoKardia Australia Pty Ltd. (Australia)

MyoKardia Netherlands B.V. (Netherlands)

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Forms S-3 (Nos. 333-223526 and 333-219220) and Forms S-8 (Nos. 333-229699, 333-222866, 333-215822, and 333-207674) of MyoKardia, Inc. of our report dated February 27, 2020 relating to the financial statements and the effectiveness of internal control over financial reporting, which appears in this Form 10-K.

PricewaterhouseCoopers LLP
San Jose, California
February 27, 2020

Exhibit 31.1

CERTIFICATIONS

I, T. Anastasios Gianakakos, certify that:

1. I have reviewed this Annual Report of MyoKardia, Inc. on Form 10-K for the period ended December 31, 2019 as filed with the Securities and Exchange Commission on the date hereof (the "Report");

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

February 27, 2020

/s/ T. Anastasios Gianakakos
T. Anastasios Gianakakos
Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATIONS

I, Taylor Harris, certify that:

1. I have reviewed this Annual Report of MyoKardia, Inc. on Form 10-K for the period ended December 31, 2019 as filed with the Securities and Exchange Commission on the date hereof (the "Report");

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

February 27, 2020

/s/ Taylor Harris
Taylor Harris
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO SECTION 906
OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of MyoKardia, Inc. (the "Company") on Form 10-K for the period ended December 31, 2019 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, T. Anastasios Gianakakos, the Chief Executive Officer of MyoKardia, Inc. (the "Company"), do hereby certify in accordance with 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002 that, based upon my knowledge:

1. This Annual Report on Form 10-K of the Company, to which this certification is attached as an exhibit (the "Report"), fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

February 27, 2020

/s/ T. Anastasios Gianakakos
T. Anastasios Gianakakos
Chief Executive Officer
(Principal Executive Officer)

A signed original of this written statement required by Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. Section 1350), has been provided to MyoKardia, Inc. and will be retained by MyoKardia, Inc. and furnished to the Securities and Exchange Commission or its staff upon request. This certification accompanies the Form 10-K to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of MyoKardia, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing.

Exhibit 32.2

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO SECTION 906
OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of MyoKardia, Inc. (the "Company") on Form 10-K for the period ended December 31, 2019 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Taylor Harris, Chief Financial Officer, Finance and Corporate Development (Principal Financial and Accounting Officer) of the Company, certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

1. The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
2. Information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

February 27, 2020

/s/ Taylor Harris
Taylor Harris
Chief Financial Officer
(Principal Financial and Accounting Officer)

A signed original of this written statement required by Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. Section 1350), has been provided to MyoKardia, Inc. and will be retained by MyoKardia, Inc. and furnished to the Securities and Exchange Commission or its staff upon request. This certification accompanies the Form 10-K to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of MyoKardia, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing.