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

FORM 10-K

☒ **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: 001-38853

NGM BIOPHARMACEUTICALS, INC.
(Exact name of Registrant as specified in its charter)

Delaware	**26-1679911**
	(I.R.S. Employer Identification No.)
(State or other jurisdiction of incorporation or organization)	

333 Oyster Point Boulevard
South San Francisco, California 94080
(Address of principal executive offices and zip code)

Registrant's telephone number, including area code: (650) 243-5555

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

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

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

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. YES ☐ 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 the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☐	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 registrant's common stock held by non-affiliates of the registrant as of June 28, 2019, the last business day of the registrant's most recently completed second fiscal quarter, was approximately $359 million, calculated based on the closing price of the registrant's common stock as reported by the Nasdaq Global Select Market. Excludes an aggregate of 41,515,530 shares of the registrant's common stock held as of such date by officers, directors and stockholders that the registrant has concluded are or were affiliates of the registrant. Exclusion of such shares should not be construed to indicate that the holder of any such shares possesses the power, direct or indirect, to direct or cause the direction of the management or policies of the registrant or that such person is controlled by or under common control with the registrant.

As of March 12, 2020, the number of outstanding shares of the registrant's common stock, par value $0.001 per share, was 67,752,589.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive Proxy Statement for the 2020 Annual Meeting of Stockholders to be filed with the U.S. Securities and Exchange Commission pursuant to Regulation 14A not later than 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K are incorporated by reference in Part III, Items 10-14 of this Annual Report on Form 10-K.

NGM BIOPHARMACEUTICALS, INC.
2019 ANNUAL REPORT ON FORM 10-K
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Unless the context suggests otherwise, references in this Annual Report on Form 10-K (the "Annual Report") to "us," "our," "NGM," "NGM Biopharmaceuticals," "we," the "Company" and similar designations refer to NGM Biopharmaceuticals, Inc. and, where appropriate, its subsidiary.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report contains forward-looking statements that involve risks, uncertainties and assumptions that, if they never materialize or prove incorrect, could cause our results to differ materially from those expressed or implied by such forward-looking statements. The statements contained in this Annual Report that are not purely historical are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. Forward-looking statements are often identified by the use of words such as, but not limited to, “anticipate,” “believe,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “will,” “would” or the negative of those terms, and similar expressions that convey uncertainty of future events or outcomes to identify these forward-looking statements. Any statements contained herein that are not statements of historical facts may be deemed to be forward-looking statements. Forward-looking statements in this Annual Report include, but are not limited to, statements about:

- the success, cost and timing of our product development activities and clinical trials;
- our or our partners’ ability to obtain and maintain regulatory approval for aldafermin (NGM282), NGM313 (MK-3655), NGM120, NGM217, NGM621, NGM395 and any of our future product candidates, and any related restrictions, limitations, and/or warnings in the label of an approved product candidate;
- our belief that aldafermin may have the potential to be a treatment for non-alcoholic steatohepatitis (“NASH”) patients with moderate to advanced fibrosis;
- our belief regarding the impact of our product candidate side effects and our ability to effectively manage these side effects;
- our belief that MK-3655 (formerly NGM313) may have the potential to be a treatment for NASH patients with early to moderate fibrosis with or without type 2 diabetes;
- the potential renewal of our research collaboration, product development and license agreement with Merck Sharp & Dohme Corp. (“Merck”; and such agreement, the “Collaboration Agreement”) and the possibility that Merck will decide to exercise its option to license certain programs upon our completion of a proof-of-concept study in humans;
- our ability to obtain funding for our operations;
- the commercialization of our product candidates, if approved;
- our plans to research, develop and commercialize our product candidates;
- our ability to attract additional collaborators with development, regulatory and commercialization expertise;
- current and future agreements with third parties in connection with the commercialization of aldafermin, NGM313, NGM120, NGM217, NGM621, NGM395 or any other future approved product;
- the size and growth potential of the markets for our product candidates, and our ability to serve those markets;
- the rate and degree of market acceptance of our product candidates, as well as the reimbursement coverage for our product candidates;
- regulatory developments in the United States and foreign countries;
- the performance of, and our ability to obtain sufficient supply of clinical trial materials in a timely manner from, third-party suppliers and manufacturers;

- the success of competing therapies that are or may become available;
- our ability to attract and retain key scientific, development and management personnel;
- our estimates regarding future expenses, revenue, capital requirements and needs for additional financing;
- our expectations regarding the period during which we qualify as an emerging growth company under the Jumpstart Our Business Startups Act of 2012, as amended (the "JOBS Act"); and
- our expectations regarding our ability to obtain, maintain, protect and enforce intellectual property protection for our product candidates.

These statements are based on the beliefs and assumptions of our management, which are in turn based on information currently available to management. Such forward-looking statements are subject to risks, uncertainties and other important factors that could cause actual results and the timing of certain events to differ materially from future results expressed or implied by such forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in the section entitled "*Risk Factors*" included under Part I, Item 1A below. Furthermore, such forward-looking statements speak only as of the date of this Annual Report. Except as required by law, we undertake no obligation to update any forward-looking statements to reflect events or circumstances after the date of such statements.

PART I

Item 1. Business.

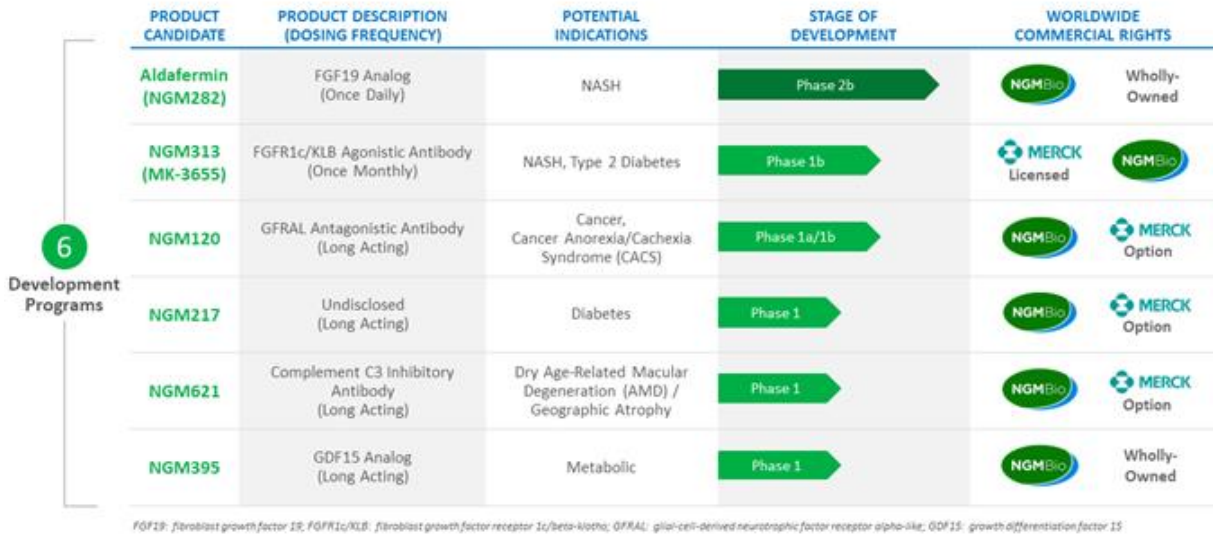
Overview

We are a clinical-stage biopharmaceutical company developing novel therapeutics based on our scientific understanding of key biological pathways underlying cardio-metabolic, liver, oncologic and ophthalmic diseases. These diseases represent leading causes of morbidity and mortality and a significant burden for healthcare systems. Since the commencement of our operations in 2008, we have generated a robust portfolio of product candidates. Our most advanced product candidate, aldafermin, is wholly-owned and entered into Phase 2b development for the treatment of NASH in 2019. Five of our other product candidates are undergoing or have completed Phase 1 clinical trials, and we have other programs in preclinical testing; some of these are subject to our Merck collaboration, as described below. We have created this portfolio using our research and drug discovery approach that employs unbiased, *in vivo*-based discovery to identify proprietary insights into critical biological processes. We combine this approach with our protein and antibody engineering expertise to find the appropriate modality to enhance each product candidate's therapeutic potential.

In 2015, we entered into a Collaboration Agreement with Merck that had an initial term of five years. In March 2019, Merck exercised its option to extend the collaboration for two additional years. The collaboration included an exclusive worldwide license to our growth differentiation factor 15 ("GDF15") program, for which Merck terminated its license effective May 31, 2019. Under the Collaboration Agreement, we also granted Merck options to take exclusive, worldwide licenses for the programs in our research and development pipeline on a program-by-program basis. Our fibroblast growth factor 19 ("FGF19") program, including aldafermin, is not included in the Collaboration Agreement, and it remains wholly-owned by us.

Merck generally has a one-time right to exercise its option to an exclusive, worldwide license when a program completes a human proof-of-concept trial. In November 2018, Merck exercised its option to license NGM313, an agonistic antibody selectively activating fibroblast growth factor receptor 1c-beta-klotho ("FGFR1c/KLB"), which is a potential treatment for NASH and type 2 diabetes. The collaboration enables us to develop more product candidates for major indications than we could likely advance on our own, with Merck bearing a majority of the associated cost and risk. We retain an option, when a candidate has advanced to Phase 3 clinical trials, to participate in up to 50% of the economic return from that candidate if it becomes an approved medicine. Overall, the Merck collaboration provides us with robust research and development support, while we retain our research independence and the option to split costs and profits on product candidates Merck elects to advance.

Our most advanced programs are focused on novel discoveries in hormone pathways that regulate cardio-metabolic processes and liver function, including those driving NASH, type 2 diabetes and obesity. We have identified multiple hormone pathways of interest, the most advanced of which are: FGF19, which plays a critical role in controlling bile acid, lipid and glucose metabolism; FGFR1c/KLB, which regulates insulin sensitivity, blood glucose and liver fat; and GDF15, which drives profound metabolic activity by regulating fuel flux and has been considered a challenging therapeutic target. We believe these hormone pathways work through distinct mechanisms and play an important role in metabolic regulation. Our six most advanced proprietary product candidates are summarized below.



We are currently focused on the following programs:

- Aldafermin is an engineered variant of the human hormone known as FGF19, which we are developing as a once-daily subcutaneous injection for the treatment of NASH. FGF19 is a highly specific and potent regulator of liver fat metabolism and bile acid synthesis that we believe is responsible for some of the beneficial effects of gastric bypass surgery on NASH. Preliminary results from Phase 2 clinical trials have provided clinical proof of concept for a once-daily injection of aldafermin by demonstrating statistically significant reductions in liver fat, liver transaminases and biomarkers of fibrosis, which has translated into improvements in liver histology and fibrosis at 12 and 24 weeks. Preliminary results from our completed 24-week placebo-controlled Phase 2 clinical trial cohort (“Cohort 4”) assessing the histological effects of 1 mg of aldafermin revealed that treatment with aldafermin led to a robust effect across all key regulatory endpoints of fibrosis improvement, resolution of NASH and the composite of both. We also commenced testing of aldafermin in a Phase 2b dose range-finding clinical trial for the treatment of NASH patients with F2 and F3 liver fibrosis (“ALPINE 2/3”) in 2019 and expect to initiate a Phase 2b clinical trial in NASH patients with compensated cirrhosis (“ALPINE 4”) in the first half of 2020. We expect topline results from the ALPINE 2/3 clinical trial in the first half of 2021. Aldafermin is not included in our Merck collaboration, and it remains wholly-owned by us.

- NGM313, also known as MK-3655, is an agonistic antibody binding KLB and has the potential as an insulin sensitizer and regulator of lipid homeostasis to be a once-monthly treatment for NASH and type 2 diabetes. NGM313 works by selectively activating the FGFR1c/KLB co-receptor complex, which regulates energy expenditure and glucose uptake in fat cells and other tissues. Preliminary data from a Phase 1b proof-of-concept clinical trial in obese insulin resistant subjects with nonalcoholic fatty liver disease (“NAFLD”), demonstrated that a single dose of NGM313 resulted in a statistically significant reduction in liver fat content (“LFC”) and improvements in multiple metabolic parameters. Merck exercised its option to license the program in November 2018. We expect Merck to initiate a Phase 2b study of NGM313 in NASH patients in the second half of 2020.

- NGM120 is an inhibitory antibody binding glial cell-derived neurotrophic factor receptor alpha-like (“GFRAL”) that is designed to block the effects of elevated GDF15 levels on cancer anorexia/cachexia syndrome (“CACS”), and, possibly, tumors. NGM120 works by selectively inhibiting the interaction between GDF15 and its cognate receptor, GFRAL, through which the autonomic nervous system and, possibly, the neuroendocrine axis influence the body’s fuel flux to propel the cachectic state, and, possibly, the tumors, in cancer patients that have high serum levels of GDF15. We completed a Phase 1 clinical trial of NGM120 in healthy volunteers that assessed its safety, tolerability and pharmacokinetic profile. This clinical trial demonstrated that NGM120 was well tolerated at all doses studied and the pharmacokinetics supported once-monthly dosing. In the first quarter of 2020, we initiated a Phase 1a/1b clinical trial to assess the anti-CACS and anti-cancer effect of NGM120 in patients with advanced solid tumors. Merck has a one-time option to license NGM120 upon our completion of a proof-of-concept study in humans.

- NGM217 is an antibody binding an undisclosed target and is designed to restore pancreatic islet function and increase insulin production in patients with diabetes. NGM217 is in a Phase 1 clinical trial to assess its safety, tolerability and pharmacokinetics in adults with autoimmune diabetes. We expect to initiate a Phase 1b/2a proof-of-concept clinical trial in adults with autoimmune diabetes to assess NGM217’s ability to increase levels of C-peptide, a biomarker of insulin production, in the second half of 2020. Merck has a one-time option to license NGM217 upon our completion of a proof-of-concept study in humans.

- NGM621 is an inhibitory antibody binding complement C3 that is designed to decrease levels of this protein implicated in the dry form of AMD, also known as geographic atrophy (“GA”). NGM621 completed investigational new drug (“IND”)-enabling studies and we initiated a Phase 1 safety, tolerability and pharmacokinetics clinical trial in patients with GA in the second half of 2019. We plan to initiate a Phase 2 proof-of-concept clinical trial in the second half of 2020. Merck has a one-time option to license NGM621 upon our completion of a proof-of-concept study in humans.

- NGM395 is an engineered variant of the human hormone known as GDF15 that has the potential to be a once-weekly or less frequent injection for the treatment of metabolic syndrome. We discovered that metabolic activity of GDF15 is mediated by GFRAL, which is located in a region of the brain stem outside the blood-brain barrier. NGM395 is designed to stimulate a pathway that modulates the autonomic nervous system and, possibly, the neuroendocrine axis to modify body weight and fat levels in the body. Merck licensed the GDF15 receptor agonist program, which included NGM395 and NGM386, a once-daily injection, and completed a Phase 1 clinical trial of NGM386 in overweight or obese but otherwise healthy adults. Preliminary data from the study indicated that NGM386 treatment for 28 days was generally well tolerated but did not result in significant body weight loss in obese subjects. Effective May 31, 2019, Merck terminated its license to the GDF15 receptor agonist program and we regained full rights to the program, which includes NGM395 and NGM386. Following our assessment of the NGM386 Phase 1 study results, we decided to suspend activities related to NGM386 and focus on advancing NGM395. We initiated a Phase 1 clinical trial to assess safety, tolerability and pharmacokinetics of NGM395 in obese but otherwise healthy adults in the first quarter of 2020.

Using our drug discovery approach, we have identified and are actively investigating over ten additional biological pathways with potential to intervene in diseases. For these pathways, we are further identifying mechanistic insights and their relevance to human biology, and generating biologic drug candidates that appropriately modulate the signals we have identified. These programs are in various stages of development, ranging from functional validation to preclinical testing. Discovery activity in selected therapeutic areas including cardio-metabolic, liver, oncologic and ophthalmic diseases is ongoing and in various stages of research.

Our Strategy

Our strategy is to leverage our biology-centric drug discovery approach to uncover novel mechanisms of action and generate proprietary insights that will enable us to move rapidly into proof-of-concept studies and deliver first-in-class medicines to patients. Key elements of our strategy are:

- ***Establish Aldafermin, Our Wholly-Owned Compound, as the Leading Treatment for NASH Patients with Moderate to Advanced Fibrosis:*** In Phase 2 clinical trials in NASH, patients taking aldafermin have experienced rapid and robust reductions in liver fibrosis, lobular inflammation, hepatocellular ballooning, liver fat and liver transaminases. These results suggest that aldafermin has the potential to resolve disease and reverse fibrosis in NASH patients with moderate to advanced liver fibrosis. We initiated the ALPINE 2/3 clinical trial in 2019 and plan to initiate the ALPINE 4 clinical trial in the first half of 2020, which will inform dose selection for a Phase 3 clinical trial in these patient populations to support a filing for initial marketing approval. As part of our life-cycle management strategy, we intend to also develop a version of aldafermin with an extended half-life, or exposure duration in the blood, which will enable less frequent dosing.

- ***Leverage Our Collaboration with Merck to Advance Our Pipeline:*** Our collaboration with Merck provides us with financial resources and access to industry-leading, late-stage clinical development and commercialization capabilities, which we believe affords us substantial freedom to pursue and achieve our vision. We intend to leverage Merck's financial support and translational expertise to accelerate and broaden our development efforts for our programs beyond aldafermin and NGM395. Our option to elect a cost and profit share for collaboration products that have advanced to Phase 3 trials preserves the potential for our substantial economic participation in such programs.

- ***Grow Our Pipeline and In Our Therapeutic Areas of Focus:*** Our initial research focus was on the biology underlying cardio-metabolic, liver, oncologic and ophthalmic diseases. Our collaboration with Merck creates an incentive for us to develop multiple candidates through human proof-of-concept studies, but does not limit the therapeutic areas that we can explore. We are working to establish human proof of concept for NGM120 in cancer, NGM217 for autoimmune diabetes and NGM621 for dry AMD, and plan to continue growing our pipeline of product candidates at our historical rate, with the goal of identifying high-impact therapeutics.

- ***Build Capabilities to Deliver Medicines to Patients in Areas of High Unmet Medical Need:*** We have worldwide rights to our lead product candidate, aldafermin. If approved, we intend to bring aldafermin to market by building our own specialty salesforce in the United States targeting hepatologists and may seek to expand our reach by leveraging partners' commercial capabilities. We believe a targeted salesforce would have the ability to deliver aldafermin to the majority of the initial target population of NASH patients with moderate to advanced fibrosis. For our other programs in the Merck collaboration, we have the option to participate in co-detailing in the United States.

- ***Strengthen Our Position as a Leading Drug Discovery and Development Company:*** We aspire to operate one of the most productive research and development engines in the biopharmaceutical industry. Our team of experienced scientists and drug developers has designated six molecules that are all in clinical development. We intend to continue growing our pipeline of experimental medicines and build on our proficiency in discovery research by continuing to expand our capabilities in protein and antibody engineering, pharmacology, translational medicine and preclinical and clinical development.

Our Approach to Drug Discovery and Development

We pursue drug discovery and development through a multi-step process geared towards translating powerful human biology into first-in-class medicines. Our founding team designed our approach based on many decades of experience in successful drug development at other companies, including Amgen, Genentech and Tularik. Our process pairs a research approach that generates novel insights into pathways demonstrating powerful biological effect with the expertise in protein and antibody engineering to transform those insights into product candidates. This process seeks to address the challenges in drug discovery in diseases that involve complex, integrated biological pathways.

Identifying Pathways of Interest

We identify target genes or pathways of interest by utilizing three approaches:

- an unbiased, *in vivo* functional evaluation system formed the foundation of our discovery efforts in metabolism and enabled us to identify and characterize novel human hormones that demonstrate profound biological effects, including FGF19 and GDF15, for which we have advanced development candidates;

- analysis of human genetics data to identify genetic markers, such as single nucleotide polymorphisms, that correlate with a particular phenotype associated with disease; and

- gene expression profiling to identify genes that are regulated by certain conditions or disease states and that may contribute to the associated pathology.

We then characterize and confirm the effects of modulating the biological activity of these potential targets using *in vivo* models designed to mimic the disease of interest. We interrogate the biological activity of candidate targets using *in vivo* models because *in vitro* experiments, which take place outside a living organism, are not capable of adequately reflecting complex biological processes and interactions that are regulated by multi-organ systems. Historically, *in vivo* screening at a scale and speed for drug discovery has not been practical as it has largely been dependent on generating purified protein for functional testing. We use recombinant adeno-associated virus ("rAAV") vectors, a proven research tool that can introduce the gene of interest directly into disease models to enable the biological function of the resultant protein to be assessed *in vivo*. With this rAAV technology, we developed an unbiased, *in vivo* functional evaluation system that formed the foundation of our discovery efforts in cardio-metabolic disease and enabled us to identify novel pathways that demonstrate profound metabolic effects. To interrogate biological function and confirm activities observed in the rAAV gene delivery studies, subsequent pharmacological evaluation of select targets is conducted in disease animal models using bioactive recombinant proteins and/or monoclonal antibodies. In addition, we utilize *in vivo* models with loss of function mutations or knockouts to understand the function of certain human genes as they relate to the disease of interest. By employing these approaches in animal models of human diseases, we can elucidate the biology of potential human drug targets in a relevant *in vivo* setting and evaluate their impact on the manifestation and progression of disease.

Translation of Pathway Biology to Product Candidates

Once a strong indication of biological activity is generated for a protein of interest, we employ a differentiated process aimed at quickly identifying a lead candidate to enable us to rapidly advance the program to evaluate the effect of these product candidates on biomarkers of disease or target activity in order to enable early demonstration of human proof of concept. We probe the mechanism of action, signaling pathways and the relationship between the protein structure and function to help inform how to translate the biological activity into a potential product candidate. Through these activities we have been able to identify novel interaction partners, their expression patterns and their signaling activities, which help elucidate biological mechanisms and inform selection of a lead candidate. We leverage our expertise in protein and antibody engineering to translate biological signals into differentiated product candidates. We have an unbiased antibody generation technology, along with an armamentarium of therapeutic protein and antibody engineering capabilities, including bispecific antibodies, bifunctional antibody fusions and methods for extending the half-lives of native proteins. This range of potential modalities not only allows us to generate a portfolio of product candidates from which to select a lead, but also provides important tools to define the biological activity of the candidates.

After we have identified a lead candidate in a program, we design our early clinical trials to provide proof of biological activity, in addition to assessing safety and tolerability, to determine whether the activity we have observed in animal models can be translated into human subjects. We believe our deep understanding of the fundamental biological mechanisms observed for our chosen development candidates and the specific relationship between structure and pharmacological function distinguish our drug discovery approach from many others applied in our industry today.

The cornerstone of our research and development approach is the experienced and talented team of scientists and drug developers who built and run it. A common theme in our team's expertise is the ability to translate biological signals in animal models into drugs with human activity. Members of our team played significant roles at prior companies in discovering and developing multiple approved drugs, including recombinant human insulin,

human growth hormone, tissue plasminogen activator and interferon alpha and gamma, as well as metreleptin and evolocumab (Repatha®). Our team seamlessly integrates discovery biology, protein and antibody engineering, preclinical development, early clinical development and manufacturing for each program. Our scientific advisory board further strengthens our experience base and includes key contributors to the discovery of the statin class of drugs, as well as thought leaders in new areas complementary to our early-stage research efforts.

Our Initial Focus on Cardio-Metabolic and Liver Disease

Cardio-metabolic and liver diseases, including NASH, diabetes and obesity, represent a leading cause of morbidity and mortality, a significant burden for healthcare systems and an area of relative underinvestment by the pharmaceutical industry. Metabolic syndrome is exhibited by 34% of adults in the United States and comprises a constellation of co-morbid conditions, including type 2 diabetes, obesity, high blood pressure, poorly regulated lipids and NAFLD, a precursor condition to NASH. Despite a wave of public health campaigns to promote better diet and exercise habits and a range of treatment options available for many of these cardio-metabolic diseases, morbidity and mortality rates remain high and more effective therapeutics are needed.

Cardio-metabolic and liver diseases represent areas of both rapidly growing unmet medical need and underinvestment, driven in part by the biological complexity of the diseases and the substantial costs necessary to develop new therapeutics. Leveraging our differentiated drug discovery approach, we have spent the last decade discovering and developing a portfolio of clinical-stage drug candidates that target various forms of cardio-metabolic disease including NASH, type 2 diabetes and obesity. Each of these drug candidates stem from novel insights we have made in understanding hormone pathways that regulate cardio-metabolic processes. Aldafermin is our lead product candidate in development for treating NASH, a cardio-metabolic liver disease. As explained below, the clinically validated, dual mechanism of action of aldafermin supports its therapeutic potential in NASH, an indication with a high prevalence and for which there are no approved treatments. Our investment in cardio-metabolic diseases was further expanded in 2015 through our collaboration with Merck, which provided resources to advance multiple programs, in addition to our wholly-owned aldafermin program. Five of our most advanced clinical candidates —aldafermin, NGM313, NGM120, NGM217 and NGM395—are notable because their preclinical profiles suggest the potential to broadly impact the drivers of various diseases with an underlying metabolic dysregulation.

Other Focus Areas

Beyond cardio-metabolic and liver diseases, we are also pursuing treatments for oncologic and ophthalmic diseases, which are also major disease categories that are growing in incidence and lack adequate treatments. NGM120 is our first product in oncology and NGM621 is our first product candidate in ophthalmic disease. All of our programs embody our focus on delivering transformative therapeutics to patients by applying our proprietary insights into powerful biology underlying major diseases.

Our Programs

Aldafermin: A Rapid and Potent Approach to Treating NASH

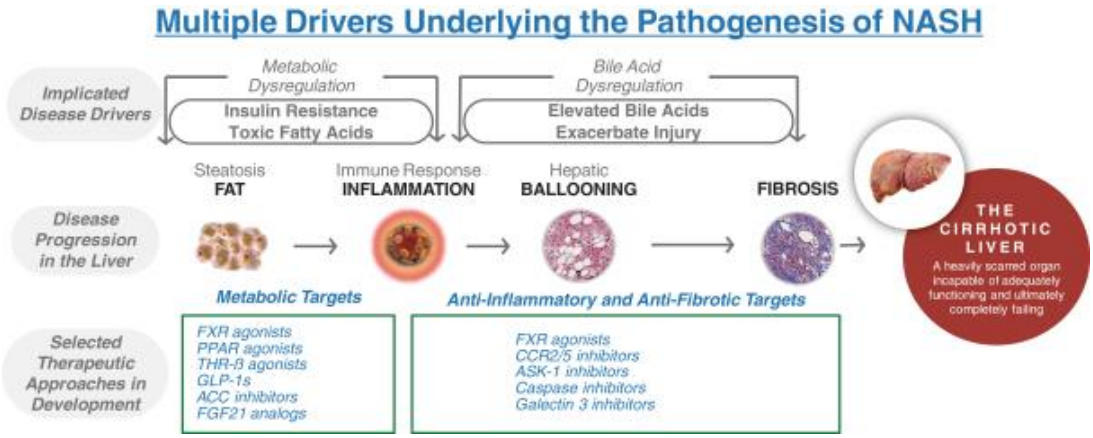
Aldafermin, an engineered version of human hormone FGF19 that is administered through a once-daily subcutaneous injection, has demonstrated the ability to rapidly improve NASH and reverse liver fibrosis in clinical and preclinical studies. We believe the combination of breadth, magnitude and speed of effect demonstrated by aldafermin in these studies results in an agent that, if ultimately approved, could provide a needed medicine for physicians to treat NASH patients with moderate to advanced fibrosis. We have tested aldafermin in over 475 subjects, including more than 200 NASH patients. We initiated the ALPINE 2/3 clinical trial in 2019 and plan to initiate the ALPINE 4 clinical trial in the first half of 2020. Aldafermin is wholly-owned and it is not subject to our collaboration with Merck.

NASH: A Progressive Metabolic and Fibrotic Disease of the Liver that Affects Millions

NASH is a life-threatening form of liver disease. It results from the progression of NAFLD, which is a common co-morbidity of the metabolic syndrome and obesity. NAFLD is characterized by abnormal amounts of fat in the liver, a condition known as steatosis, and is often associated with insulin resistance. This abnormal fat in the liver contributes to the progression in certain NAFLD patients to NASH by developing a necroinflammatory state in the liver that ultimately drives scarring, also known as fibrosis, and, for many, progresses to liver failure, also known as cirrhosis.

The estimated global prevalence of NAFLD and NASH has risen rapidly in parallel with the dramatic rise in population levels of obesity and diabetes. NAFLD now represents the most common cause of liver disease in the Western world. In the United States alone, the prevalence of NASH was estimated to total 16.5 million cases and is projected to reach 27 million cases by 2030, with similar trends occurring globally. The annual economic burden associated with NAFLD and NASH in the United States was estimated to have been over $100 billion in 2016.

Although the mechanism underlying the development and progression from simple steatosis to NASH and cirrhosis is poorly understood, insulin resistance and inflammatory mediators, including lipotoxicity, cytokines and oxidative stress, are believed to promote the development of NASH and its extrahepatic complications. Excess lipotoxic, or fat, metabolites in the liver are believed to provide the primary insult in the pathogenesis of NASH, and several treatments are in development targeting mechanisms to reduce these disease drivers. Other treatments in development aim to reduce the inflammatory and fibrotic damage created by this metabolic dysregulation. Evidence also supports a role for bile acids in the pathogenesis of liver inflammation and fibrosis. Accumulation of bile acids, in particular, more toxic hydrophobic bile acids, within hepatocytes can cause mitochondrial dysfunction, endoplasmic reticulum stress and immune cell infiltration that can ultimately lead to inflammation, cell death and liver injury.



Most patients with NASH are diagnosed in their forties or fifties; however, NASH develops across all ages, including in children, which is thought to be linked to an increase in childhood obesity. Most NASH patients are asymptomatic, although some may present with fatigue, malaise and vague right-upper abdominal discomfort. Patients are more likely to be initially identified by elevated liver aminotransferases on routine lab tests or hepatic steatosis detected incidentally on abdominal imaging. While non-invasive diagnostic tools are under development, a definitive diagnosis of NASH is currently only achievable through liver biopsy to assess the components of the NAFLD activity score ("NAS").

The histologic criteria for the diagnosis of adult NASH include steatosis, lobular inflammation and hepatocellular ballooning. Portal and periportal fibrosis followed by bridging fibrosis and cirrhosis are seen in patients as NASH progresses. Physicians assess the severity of NASH by liver biopsy using two different scoring systems, the NAS and the fibrosis stage (F0 to F4). The tables below describe the scoring criteria of the two systems:

NAFLD Activity Score System

Component	Score	Thresholds
Steatosis (% of microscopic field showing steatosis)	0	<5%
	1	5-33%
	2	>34%-66%
	3	>66%
Lobular Inflammation (Number of immune cell foci per 20x optical field in microscope)	0	None
	1	<2 foci
	2	2-4 foci
	3	>4 foci
Hepatocellular Ballooning (amount of ballooning cells in microscopic field)	0	None
	1	Few cells
	2	Many cells
Total NAS Score = steatosis score + lobular inflammation score + hepatocellular ballooning score		

Fibrosis Score

Fibrosis Stage	Description
F0	Absence of fibrosis
F1	Perisinusoidal or periportal
F2	Perisinusoidal and periportal
F3	Bridging fibrosis
F4	Cirrhosis

The NAS is a validated score of liver histology that is used to grade disease activity in patients with NAFLD and NASH. The NAS is the sum of the liver biopsy's individual scores for steatosis (0–3), lobular inflammation (0–3) and hepatocellular ballooning (0–2), with fibrosis (F0–F4) scored separately. Advanced liver fibrosis is generally considered fibrosis stage F3 and F4, which may ultimately lead to end-stage liver disease, liver cancer, liver transplant and/or death.

U.S. Food and Drug Administration ("FDA") Draft Industry Guidance on NASH Drug Development and Endpoints

There are no FDA-approved therapeutics for NASH. The FDA has provided draft guidance to the industry regarding acceptable development pathways for investigational NASH agents as follows:

- the agent must be tested in NASH patients, typically characterized as having a NAS of four or greater and at least one point in each component, with F2 or F3 fibrosis;

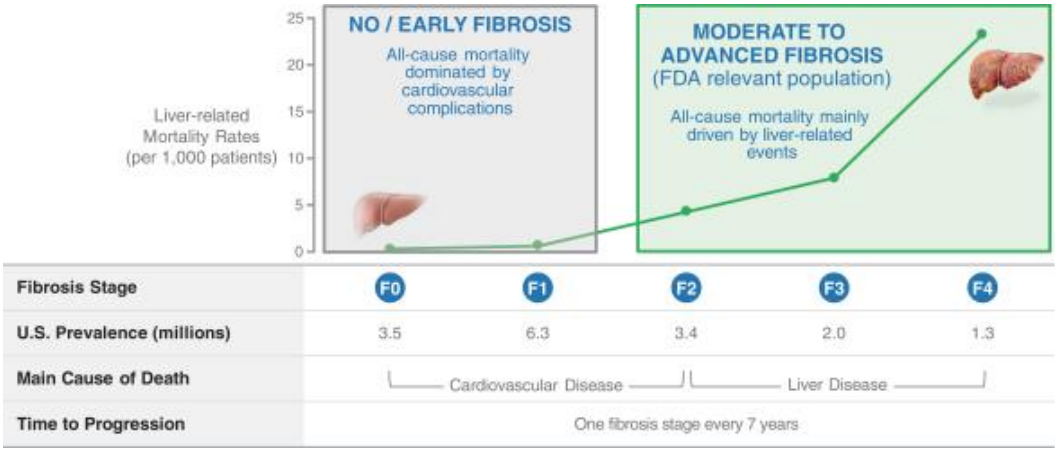
- for an accelerated approval path (Subpart H (drugs)/Subpart E (biologics)), a surrogate endpoint that is "reasonably likely to predict clinical benefit" is acceptable. A subsequent post-marketing confirmatory outcomes study is then required to be conducted to maintain licensure; and

- for a Subpart H/E approval, three biopsy-based surrogate endpoints are endorsed by the FDA, defined as the proportion of patients that achieve:
    - resolution of NASH, defined as a lobular inflammation score = 0 or 1 and a hepatocellular ballooning score = 0, with no worsening of fibrosis; or
    - one stage improvement in fibrosis with no worsening of NASH; or
    - resolution of NASH and improvement in fibrosis (as defined above).

We believe many agents in development for NASH will opt for a Subpart H/E accelerated approval pathway and rely on surrogate endpoints for initial approval. As detailed further below, fibrosis stage is currently the only measurement that is correlated to liver outcomes and, therefore, the potential for many agents that will rely only on the resolution of a NASH surrogate endpoint to demonstrate clinical benefit will remain uncertain until a confirmatory outcomes study is successfully completed.

Stage of Fibrosis Predictive of Outcomes for NASH Patients

The presence of fibrosis is the only factor that is highly predictive in identifying those patients who will progress to cirrhosis. The natural history of NASH is variable from patient to patient and, while the NAS is a valuable tool for diagnosing the disease, it does not appear to be predictive of disease progression. Of the estimated 64 million patients in the United States with NAFLD, approximately 10%–20% will progress to NASH over time. Of these NASH patients, approximately 10%–15% will progress to cirrhosis by advancing one fibrosis stage approximately every seven years. The mortality rate of NASH patients with fibrosis has been estimated at 1.5%–3.5% per year, largely due to cardiovascular disease, followed by liver-related causes. However, patients with F2 or greater fibrosis stage have a greater chance of liver-related mortality than cardiovascular-related mortality, and each stage of worsening of fibrosis correlates to an exponential increase in liver-related mortality rates. Patients with F3 and F4 fibrosis have an approximately 17 times greater risk and 42 times greater risk, respectively, of liver-related mortality than those NASH patients without fibrosis. Therefore, it is expected that treatments that can drive the regression of fibrosis are more likely to have a meaningful impact on clinical outcomes for NASH patients with F2 to F4 fibrosis.



Current Treatments

Currently, no agents have been approved for the treatment of NASH. Weight loss through diet and lifestyle management is currently considered the first-line treatment strategy for NASH and is associated with improvement in liver histology and a reduction in cardiovascular and metabolic complications. However, fewer than 10% of patients are successful in achieving or maintaining at least a 10% total body weight loss that is sufficient to improve fibrosis and, therefore, require other interventions. In cases of morbid obesity, gastric bypass surgery has been successful in resolving NASH in a majority of patients; however, the effect on fibrosis improvement was less substantial and the risk of complications and expense of the surgery limit more widespread use.

In the absence of approved products, some physicians utilize agents approved for other indications, including Vitamin E and pioglitazone; however, the evidence of their effect on NASH is modest and/or they have safety issues that limit acceptance. Given the increasing disease burden and lack of approved treatment options, the development of novel pharmacologic therapies to treat NASH is critical.

Treatments in Development

While there are many agents in clinical development for NASH, the landscape can be subdivided into a few mechanistic classes based on the putative disease drivers they target. Most treatment approaches for NASH have focused on the prevention or reversal of liver injury either by predominantly treating the metabolic dysregulation of the disease or through directly targeting inflammatory or fibrogenic pathways. NASH is a chronic, slowly progressing disease and, currently, many believe that slowing the progression or reversing disease requires treatment periods of at least 12 months. To attempt to overcome modest individual agent activity, combination therapy is being pursued by some NASH drug developers on the theory that the complex underlying pathophysiology of NASH will require targeting multiple mechanisms to achieve a sufficient disease-modifying effect to be clinically relevant.

Drug Candidates Pursuing a Metabolic Approach to Treating NASH

Certain NASH drug development candidates are focused on the metabolic components of the disease, such as insulin resistance and lipotoxicity that are associated with the inception and early stages of the disease pathology. The rationale for these treatment candidates is based on an expectation that the improvement of the underlying liver insult of metabolic dysregulation will allow the liver to recover over the long term, which would potentially allow the liver to repair itself and eventually improve fibrosis. Although clinical data for some compounds in this mechanistic class show a beneficial effect on steatosis and an improvement in the NAS, the effect on fibrosis is likely to be highly dependent on the compound being tested. Any of these metabolic-focused compounds that are ultimately approved may be appropriate to halt the progression of disease in earlier-stage NASH patients or used in combination with other agents. Considering the correlation of liver failure outcomes with fibrosis stage, we believe the NASH patients with moderate to advanced fibrosis (F2 to F4) will require a more potent and fast-acting agent to prevent the progression to end-stage liver disease.

Drug Candidates Pursuing an Anti-Inflammatory and/or Anti-Fibrotic Approach to Treating NASH

Candidates targeting various mechanisms with possible anti-inflammatory and anti-fibrotic effects are also in clinical testing for NASH. These classes of compounds have shown mixed results in meaningfully improving the fibrosis score of patients. Where fibrosis improvements have been shown, results have either been transient or not accompanied by significant improvements in other histological measures of the disease. These classes of compounds have also shown limited ability to improve NASH.

We believe the minimal efficacy on fibrosis improvement and lack of activity on resolving NASH that has been observed to date with anti-inflammatory and anti-fibrotic agents may reflect the difficulty in treating the disease without removing the underlying insult of lipotoxicity, or the challenge of impinging on the complex process of hepatocellular death and fibrosis from collagen deposition by intervention through a single pathway.

Drug Candidates with Multiple Mechanisms

To date, drug candidates with multiple mechanisms of activity have shown the most promising effect on NASH. The FXR agonist, obeticholic acid (“OCA”), demonstrated improvements in the NAS and fibrosis, but not resolution of NASH as defined by the Phase 2 and Phase 3 study protocols. FXR agonists are known to regulate hundreds of genes, and one of the factors upregulated is FGF19. We believe FGF19 is the primary mediator of the activity of FXR agonists in NASH. FXR agonists are limited, however, in the magnitude of FGF19 levels they can achieve by the boundaries of normal physiology. We believe this limitation to sub-pharmacological levels of FGF19 will limit the ability of FXR agonists to produce a meaningful effect in NASH, in the same way that insulin secretagogues have mild activity compared to insulin itself in treating diabetes. Additionally, treatment with OCA and other FXR agonists has been associated with pruritus, or whole body itching, which can cause patients to discontinue treatment. There are multiple FXR agonists in preclinical or clinical development seeking to improve on the properties of OCA; however, we believe their activity on NASH will be limited by their inability to sufficiently elevate FGF19 levels over a sustained period of time and/or their utility will be reduced by side effects. A New Drug Application (“NDA”) for OCA was filed with the FDA in September 2019 and the completion of their review is expected in June 2020.

To our knowledge, aldafermin is the only program in clinical development for NASH directly activating the native FGF19 pathway to drive both a regression of fibrosis and resolution of NASH.

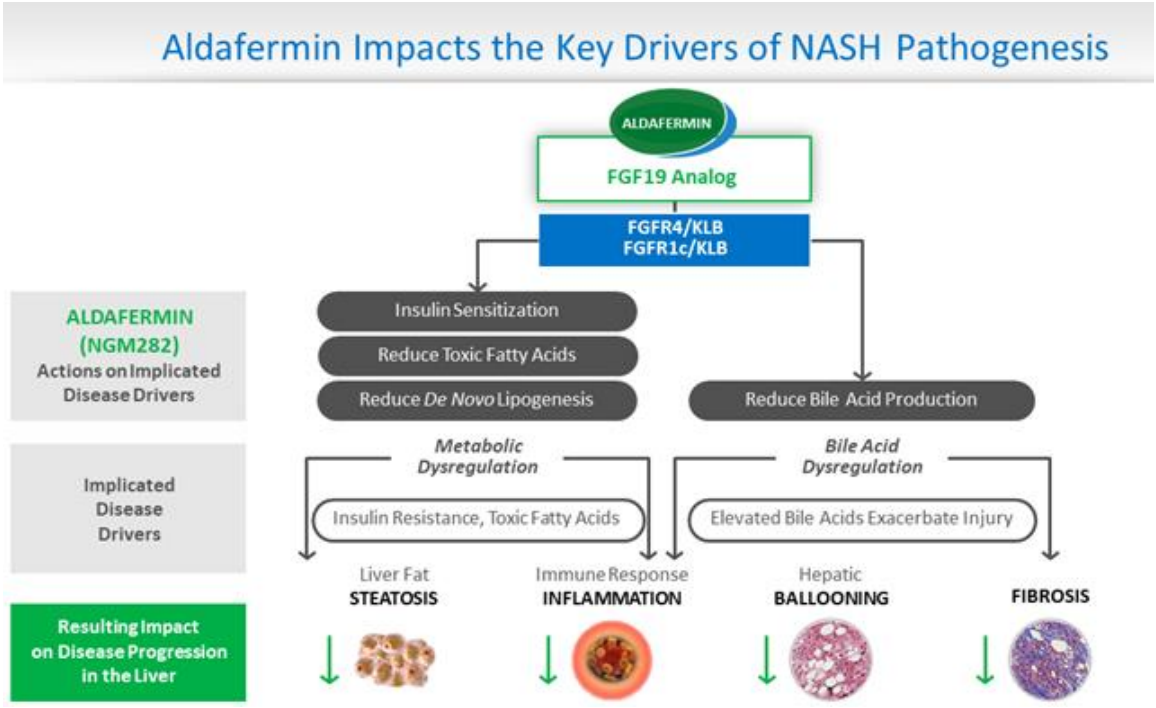
Aldafermin: A rapid and potent approach to treating NASH

Aldafermin, an engineered version of human hormone FGF19 that is administered through a once-daily subcutaneous injection, has demonstrated the ability to rapidly improve NASH and reverse liver fibrosis in clinical and preclinical studies. We believe the combination of breadth, magnitude and speed of results demonstrated by aldafermin in these studies suggests an agent that, if ultimately approved, could provide a needed medicine for physicians to treat NASH patients with moderate to advanced fibrosis. We have tested aldafermin in over 475 subjects, including more than 200 NASH patients. We initiated the ALPINE 2/3 clinical trial in 2019 and plan to initiate the ALPINE 4 clinical trial in the first half of 2020. We obtained Fast Track designation for aldafermin for the treatment of NASH and primary biliary cholangitis (“PBC”) in adults. See “Government Regulation and Product Approval—Accelerated Approval Requirements.” Aldafermin is wholly-owned by us and it is not subject to our collaboration with Merck.

In a study, gastric bypass surgery led to a resolution of NASH in approximately 80% of patients studied. We initially identified FGF19 using our rodent gastric bypass surgery model that was designed to discover hormones that may drive the beneficial metabolic effects observed following this type of surgery. We also demonstrated that serum levels of FGF19 are significantly increased in humans after gastric bypass surgery. FGF19 acts as an endocrine hormone to regulate systemic carbohydrate and energy homeostasis, similar to insulin, and also inhibit the production of bile acids in the liver. Systemic FGF19 levels are decreased in patients with NASH, type 2 diabetes or metabolic syndrome, and are normalized after gastric bypass surgery in diabetic human subjects.

The spectrum of activities ascribed to FGF19 appears to be mediated primarily through two different receptor complexes: fibroblast growth factor receptor 4-beta-klotho (“FGFR4/KLB”) and FGFR1c/KLB. FGFR4/KLB receptor complexes are found primarily in the liver and FGFR1c/KLB receptor complexes are found primarily in adipose tissue and the central nervous system. When activated, FGFR4/KLB inhibits the expression of the cholesterol 7alpha-hydroxylase 1 (“CYP7A1”) gene, which modulates bile acid production through the classical pathway in the liver. There is increasing evidence supporting the role of bile acids as a pathophysiological driver of NASH. Individuals with NASH are reported to have elevated hepatic and circulating concentrations of bile acids, as well as increased concentrations of fecal and urine bile acids. As NASH patients progress to F2 and F3 fibrosis stages, serum levels of bile acids double as compared to healthy volunteers. Furthermore, serum levels of FGF19 are increasingly depressed as fibrosis levels increase in NASH patients as compared to healthy volunteers. A combination of activities from FGFR4/KLB and FGFR1c/KLB are believed to promote multiple beneficial metabolic effects in the liver and systemically, including improved insulin sensitization, a reduction in *de novo* lipogenesis and an increase in fatty acid oxidation.

We designed aldafermin as an analog of human FGF19 to improve the drug-like properties of the protein, remove a tumorigenic signal observed in rodents and retain the beneficial properties of triggering the FGFR4/KLB and FGFR1c/KLB pathways. We believe this tandem receptor-complex activation enables an improvement in the metabolic function of the liver and reduction in bile acid synthesis, which, in turn, enables aldafermin to have a more rapid and direct impact on fibrosis as compared to other agents that only address the metabolic dysfunction of NASH, as illustrated in the figure below.



Our Clinical Experience with Aldafermin

Our clinical development program for aldafermin was designed to first assess safety and tolerability of the agent and then test for activity in humans in a variety of disease settings we believed may benefit from the signaling activity of the FGF19 pathway. Each of these trials has provided insights into the agent's activity in humans and informed our development plans for NASH. A consistent profile of activity and tolerability has emerged for the compound across these studies.

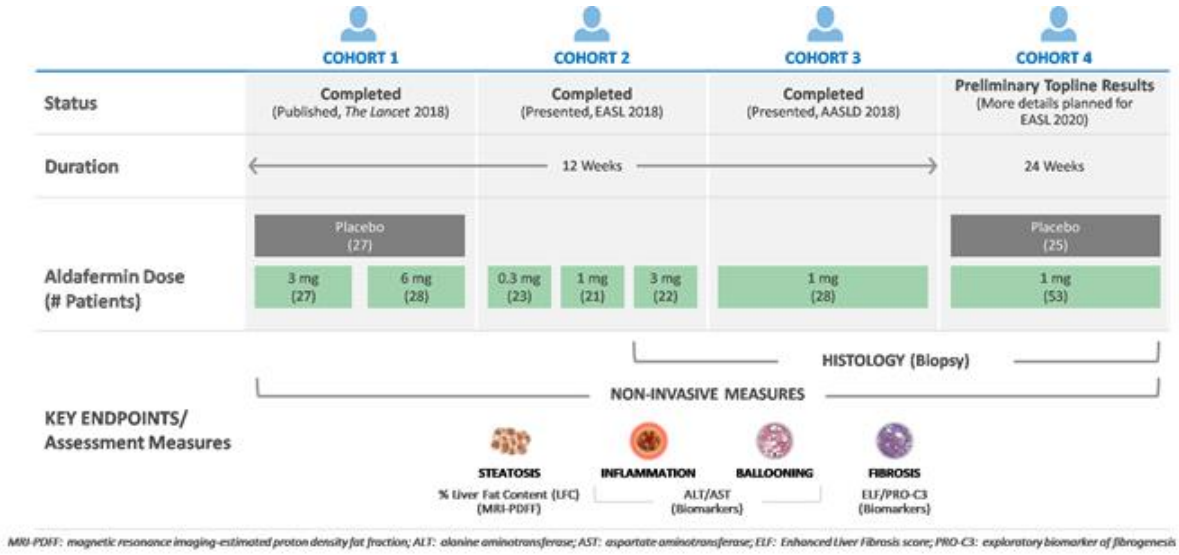
After a Phase 1 clinical trial to assess safety and tolerability, we conducted a Phase 2 clinical trial in type 2 diabetes patients to assess the impact of aldafermin on insulin resistance and blood glucose levels. Although they were not histologically confirmed for NASH, the characteristics of many of the patients enrolled in this study are consistent with a population of presumptive NASH patients as they demonstrated many of the hallmarks of NASH, including elevated levels of the liver transaminases known as alanine transaminase ("ALT") and aspartate transaminase ("AST"). This trial validated the metabolic pathways of the drug by demonstrating improvements in many metabolic parameters across the patient population, but did not result in significant blood glucose lowering after 28 days of treatment. A consistent improvement in ALT and AST was observed for patients on treatment with aldafermin, which suggested the agent was having a beneficial effect on liver health and, therefore, could have application in the treatment of NASH.

We have also explored the utility of aldafermin-mediated bile acid synthesis inhibition in two cholestatic diseases, PBC and primary sclerosing cholangitis (“PSC”), but have decided not to pursue further development of aldafermin in these diseases at this time. Although we do not currently intend to pursue aldafermin for the treatment of PBC or PSC, we previously obtained orphan drug designations for aldafermin for the treatment of PBC in adults in the United States and PBC and PSC in adults in the European Union (“EU”). See “Government Regulation and Product Approval—Orphan Drug Designation.” Both of these conditions are believed to have a strong bile acid component underlying the disease. Aldafermin achieved a significant reduction in alkaline phosphatase (“ALP”), an FDA-validated biomarker of disease in PBC, however, we determined the once-daily injectable nature of the product and competitive landscape compared to other development paths for aldafermin was not optimal. Similarly, in PSC, aldafermin treatment resulted in sustained reductions in exploratory biomarkers of fibrosis, PRO-C3 and Enhanced Liver Fibrosis (“ELF”) score, although there was no benefit in the primary endpoint of the trial, ALP. The FDA has not provided guidance on a development path for PSC that does not involve ALP and, therefore, we have determined not to move forward in this indication until a clear path is defined. Notably, PSC patients have a normal LFC level and the indication of fibrosis improvement in this population supports a role for the activity of a bile acid inhibitor, such as aldafermin, as an anti-fibrotic in the liver.

Aldafermin Phase 2 Trial in NASH Patients

Our Phase 2 clinical trial in patients with histologically-confirmed NASH included an initial double-blind placebo-controlled cohort (cohort 1), followed by a series of adaptive, open-label, single-blind cohorts evaluating 12 weeks of treatment (cohorts 2 and 3) and a double-blind, placebo-controlled study with liver biopsies at baseline and following 24 weeks of treatment (Cohort 4). Cohort 1 was designed to measure LFC by magnetic resonance imaging proton density fat fraction (‘MRI-PDFF”) and serum biomarker data at 12 weeks. This portion of the study generated distinct signals of therapeutic benefit and appropriate tolerability characteristics, which subsequently informed the adaptive cohorts 2 and 3. The open-label, single-blind 12 week cohorts (cohorts 2 and 3) were designed to explore additional dose levels of aldafermin, as well as confirm the impact of aldafermin on liver histology, as defined by improvements in fibrosis and NAS. Additionally, the protocol was amended to study statin use for those patients that experienced a low density lipoprotein (“LDL”) cholesterol increase during the first two weeks of aldafermin treatment, as further described below.

Components of the aldafermin Phase 2 Clinical Trial in NASH



MRI-PDFF: magnetic resonance imaging-estimated proton density fat fraction; ALT: alanine aminotransferase; AST: aspartate aminotransferase; ELF: Enhanced Liver Fibrosis score; PRO-C3: exploratory biomarker of fibrogenesis

Aldafermin activity has been measured across a variety of imaging and serum biomarker measures, or non-invasive measures, as well as histological measures in order to provide a comprehensive assessment of the drug's activity on NASH disease pathology. For each of cohorts 1-4, the primary endpoint was the absolute change from baseline to end of treatment in LFC. Responders were defined as patients who achieved a 5% or larger reduction in absolute LFC as measured by MRI-PDFF. Key secondary endpoints included assessments of safety and tolerability, percentage change from baseline (or relative change) in absolute LFC, normalization of LFC to less than 5% and changes from baseline and normalization in ALT and AST. Exploratory endpoints included the evaluation of biomarkers of NASH pathogenesis and fibrosis, as well as assessment of changes in liver histology in a sub-population of patients (3 mg dose group in cohort 2, 1 mg dose group in cohort 3 and all patients in Cohort 4). The table below summarizes the preliminary data generated to date and demonstrates the consistent effect across each of the non-invasive measure of NASH in each of cohorts 1-4 of this Phase 2 clinical trial, followed by a matrix explaining the significance of each of the metrics and biopsy measurements:

Aldafermin Significantly Impacts Key Parameters Consistent with Improvements in NASH

Parameter	1 DOUBLE BLIND Δ(W12-D1)			2 OPEN LABEL Δ(W12-D1)			3 OPEN LABEL Δ(W12-D1)	4 DOUBLE BLIND Δ(W24-D1)	
	Placebo (N=27)	3 mg (N=27)	6 mg (N=26)	0.3 mg (N=23)	1 mg (N=21)	3 mg bx (N=19)	1 mg bx (N=28)	Placebo (N=25)[1]	1 mg bx (N=52)[1]
MRI-PDFF, Absolute %	-0.9%	-9.7%	-11.9%	-5.3%	-11.0%	-11.2%	-10.8%	-2.7%	-7.7%
Absolute decrease ≥5% (% patients)	7%	74%	79%	57%	90%	100%	92%	24%	68%
MRI-PDFF, Relative %	-1%	-47%	-61%	-29%	-57%	-67%	-57%	-13%	-39%
Relative decrease ≥30% (% patients)	7%	85%	92%	48%	85%	100%	88%	29%	66%
ALT, Absolute (IU)	-2	-35	-33	-21	-43	-53	-63	-7	-41
ALT, Relative %	-1%	-43%	-45%	-30%	-58%	-60%	-66%	-6%	-49%
Pro-C3, Absolute (ng/ml)	-1.2	-5.4	-3.6	-2.1	-4.7	-11.1	NA	-1.2	-5.4
Fibrosis improvement, without worsening of NASH (% of patients)	NA	NA	NA	NA	NA	42%	25%	18%	38%
Resolution of NASH, without worsening of fibrosis (% of patients)	NA	NA	NA	NA	NA	11%	13%	9%	24%

Preliminary results
1 Per protocol, liver histology endpoints were assessed in the liver histology population: placebo (n=22) and aldafermin (n=50)

A description of the key non-invasive and histological measurements collected in this trial is included in the table below:

Disease Marker	Type of Measurement	Correlation with Disease Severity or Drug Activity
LFC (MRI-PDFF)	Imaging biomarker	≥5% absolute LFC reductions correlated with a 2-point NAS score reduction; ≥30% relative reduction in LFC correlated with NAS score improvement and fibrosis improvement
Liver Transaminases (ALT/AST)	Serum biomarker	Increases associated with hepatic inflammation and injury due to lipotoxicity, bile acids or other pathways
PRO-C3	Serum biomarker	A protein fragment associated with collagen deposition in the fibrogenesis process. Higher PRO-C3 is correlated with more severe fibrosis
NAFLD Activity Score (NAS)	Histology	Used as a validated measure of NASH disease severity, usually requiring at least one point in each of steatosis, lobular inflammation and hepatocellular ballooning to define having NASH; not correlated with patient outcomes
Liver Fibrosis	Histology	Severity of fibrosis is directly correlated with patient outcomes (e.g., cirrhosis and hepatocellular carcinoma, or HCC)

Cohorts 2 and 3, summarized in more detail below, included patients who received liver biopsies after 12 weeks of treatment with either 1 mg or 3 mg of daily aldafermin to enable an assessment of any improvements in histological measures of NASH, such as fibrosis. Cohort 4 included patients who received liver biopsies after 24 weeks of treatment with either 1 mg aldafermin or placebo. Preliminary data from the 3 mg dose group of cohort 2, the 1 mg dose group of cohort 3 and Cohort 4 demonstrated that aldafermin has an impact on fibrosis improvement without worsening of NASH, with 42%, 25% and 38%, respectively, registering at least a one-stage improvement in fibrosis in as early as 12 and 24 weeks. In addition, in Cohort 4, 24% of patients in the aldafermin treatment arm achieved the endpoint of resolution of NASH with no worsening of liver fibrosis as compared to 9%

of placebo patients. Of note, 22% of patients in the aldafermin treatment arm versus 0% in the placebo arm achieved the composite endpoint of both fibrosis improvement and resolution of NASH, which was statistically significant. We believe these histology results offer compelling support for aldafermin's potential as a rapidly-acting agent for NASH patients with moderate to advanced fibrosis.

Aldafermin Phase 2 Clinical Trial in NASH Patients: Cohort 1

In this double-blind cohort of the Phase 2 clinical trial, 82 subjects with biopsy-confirmed NASH were randomized to aldafermin clinical doses of 3 mg or 6 mg (n = 55) or placebo (n = 27), administered as a daily subcutaneous injection for 12 weeks. Histologic inclusion criteria included biopsy-proven NASH with a NAS 4 (at least 1 point in each component), F1 to F3 fibrosis and 8% LFC.

As published in *The Lancet* in 2018, significant reductions in absolute and relative LFC were seen with both doses, with 79% of the 6 mg-treated subjects and 74% of the 3 mg-treated subjects meeting the primary endpoint of 5% reduction in absolute LFC as measured by MRI-PDFF. There was no significant difference in absolute LFC reduction between the 3 mg and 6 mg doses. Normalization of absolute LFC (defined as $\leq$ 5% measured by MRI-PDFF) was observed in 26% and 39% of subjects treated with 3 mg and 6 mg, respectively, at week 12. Over 85% of aldafermin treated subjects achieved a decrease in relative LFC of $\geq$ 30%, which has been correlated to improvements in histology in several studies. These results were maintained across key baseline characteristics of gender (male *vs*. female), ethnicity (Hispanic *vs*. Non-Hispanic), diabetic status, ALT levels (< *vs*. $\geq$ 40 U/L), body mass index ("BMI") (< *vs*. $\geq$ 30), fibrosis stage (F1 *vs*. F2/F3) and statin use, with no significant difference in any sub-category.

Greater reductions from baseline in mean absolute ALT levels were observed for both aldafermin 3 mg (-35 international units ("IU"), p<0.0001) and 6 mg (-32 IU, p<0.0001) clinical doses at week 12 as compared with placebo. The p-value is a measure that states the probability that a comparable or better result would be produced purely by chance. A p-value of less than 0.05 means that if the drug was only as effective as the placebo, there would be less than a 5% chance that a comparable or better result would be produced purely by chance. Differences with a p-value of less than 0.05 are generally considered statistically significant, indicating a high degree of confidence that the result is due to therapy with the drug and not due to chance. This decrease in ALT levels achieved statistical significance as early as week one, with a sustained reduction throughout the entire 12-week study treatment period. The mean relative percentage decreases in ALT levels from baseline to week 12 were also significant in both doses, ranging from 43% to 44% (p<0.001). ALT levels achieved normalization (defined as <19 IU in females and < 30 IU in males) in 24% of aldafermin-treated patients by week 2 and 36% of treated subjects by week 12. Similarly, treatment with aldafermin resulted in significant mean absolute reductions in AST levels from baseline to week 12 as compared with placebo, with the majority of subjects decreasing below 40 IU as early as two weeks after starting treatment. We believe the potent and sustained inhibitory effect that aldafermin has on the classical bile acid synthesis pathway is important to achieving this rapid therapeutic effect. FXR agonists can only elevate FGF19 to the upper end of normal physiological levels, which we believe is insufficient to achieve the complete and sustained inhibition of the classical bile acid pathway.

PRO-C3 levels, as well as levels of propeptide of type III procollagen ("PIIINP") and TIMP metallopeptidase inhibitor 1 ("TIMP-1"), which are components of the ELF score, were reduced in the treated subjects, supporting a potential anti-fibrotic effect. Notably, more than 74% of aldafermin-treated subjects achieved a reduction in PRO-C3 levels of 15% at 12 weeks, as compared to 24% of placebo-treated subjects. The overall ELF score for the 3 mg- and 6 mg-treated subjects was reduced by an average of 0.3 and 0.2, respectively, compared to no change for the placebo group.

Triglyceride level decreases were consistent with FGFR1c/KLB activity triggered by aldafermin, while significant LDL cholesterol increases reflect potent FGFR4/KLB-mediated CYP7A1 inhibition. There were highly significant correlations between decreases in LFC and reductions in the serum levels of ALT, AST and C4.

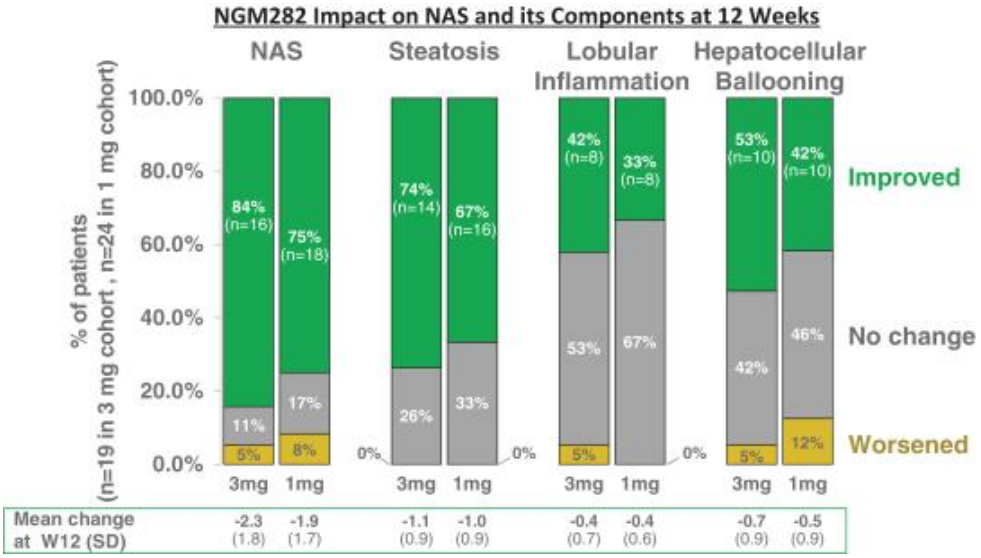
Aldafermin Phase 2 Clinical Trial in NASH Patients: Cohort 2 and 3 Imaging and Biomarker Results

Based on the impact seen with aldafermin in NASH patients across the measured non-invasive parameters assessed in cohort 1, an adaptive, open-label, single-blind cohort of three dosing groups known as cohort 2 was added to evaluate: 1) lower doses of aldafermin (0.3 and 1 mg); 2) histologic response at 12 weeks in a 3 mg dose group; and 3) the ability of concomitant statin use to mitigate drug-induced LDL cholesterol elevations. Cohort 3 was added to evaluate histologic response at 12 weeks in a 1 mg dose group. Additional MRI-PDFF images were collected at week 6 to further assess the potential for LFC responses at an earlier point in time and to evaluate the persistence of response at week 18 (six weeks after the end of treatment). The demographics and baseline patient characteristics of cohorts 2 and 3 were similar to those in cohort 1. Preliminary data for the 3 mg dose in Cohort 2 and 1 mg dose in Cohort 3 include only those patients who completed treatment with paired biopsies at baseline and week 12. Preliminary data from cohort 2 demonstrates that a significant amount of the decrease in LFC occurs by week 6 and further consolidates towards normalization at week 12 in the 1 mg and 3 mg dosing groups. The 1 mg and 3 mg dose groups in cohort 2, and the 1 mg dose group in cohort 3, showed similar reductions of LFC and ALT levels, and were consistent with the week 12 changes observed with the 3 mg dose in cohort 1. Preliminary data from the 1 mg and 3 mg dose groups in cohort 2 and the 1 mg dose group in cohort 3 also had statistically significant reductions from baseline in PRO-C3 levels (-4.7, -11.1 and -4.5 ng/ml, respectively, $p<0.05$) and PIIINP (-2.0, -3.3 and -3.2 ng/ml, respectively, $p<0.001$) and TIMP-1 (-33.1, -42.7 and -38.4 ng/ml, respectively, $p<0.05$) components of the ELF score at week 12. Based on the reductions in LFC, levels of ALT and the fibrosis markers, the 0.3 mg dose group in cohort 2 demonstrated a reduced treatment response overall as compared to the 1 mg and 3 mg dose groups of cohort 2 and the 1 mg dose group of cohort 3. Preliminary data indicates that, six weeks after the end of aldafermin treatment, the relative levels of LFC and ALT levels remained suppressed, with reductions approximately 20% to 39% and 18% to 44% below baseline levels across doses evaluated in cohorts 2 and 3, respectively. Similarly, reductions in PRO-C3 levels and ELF score components in aldafermin-treated patients were sustained six weeks after the end of aldafermin treatment.

Aldafermin Phase 2 Clinical Trial in NASH Patients: Cohort 2 (3 mg) and Cohort 3 Preliminary Histology Results

Liver histology was evaluated at 12 weeks in the 3 mg dosing group of cohort 2 and in the 1 mg dosing group of cohort 3. Each of these cohorts enrolled primarily NASH patients with moderate to advanced fibrosis. Eighty-four percent of the 19 patients in the 3 mg dosing arm of cohort 2 had been diagnosed with F2 or worse fibrosis at baseline. Eighty-three percent of the 24 patients in cohort 3 had F2 or worse fibrosis at baseline. Liver biopsies at baseline and 12 weeks were blinded by both patient and treatment sequence. They were subsequently read by a central independent liver hepatopathologist using the NASH CRN criteria. Preliminary data from cohorts 2 and 3 showed improvements in fibrosis scores in both groups, with 42% of patients in the 3 mg dosing group of cohort 2 and 25% of the patients in cohort 3 improving by at least one stage, and a mean change of -0.5 and -0.1 fibrosis stage, respectively. All of the patients experiencing improvements in fibrosis scores were F2 or worse at baseline. Between the two cohorts, a total of four patients achieved a two stage improvement in fibrosis during the 12 weeks of treatment (three in the 3 mg dosing group of cohort 2 and one in cohort 3). There were two subjects in the 3 mg dosing group of cohort 2 who worsened by one stage in fibrosis (Stage 1b to 2 and Stage 3 to 4), with no substantive worsening of their NAS and reductions in LFC and ALT. Four patients in cohort 3 worsened by one stage in fibrosis. While each cohort involved a relatively small number of patients, these preliminary results demonstrated, for the first time, the possibility of improving fibrosis in F2 to F4 NASH subjects in as early as 12 weeks of treatment with a therapeutic agent. In addition, the patients with fibrosis improvements also had a mean reduction in NAS of 3.5 and 3.2 in the 3 mg dosing group of cohort 2 and cohort 3, respectively.

At 12 weeks, aldafermin treatment resulted in resolution of NASH, defined as having a lobular inflammation score of 0 or 1 and a hepatocellular ballooning score of 0, with no worsening of fibrosis, in two patients in the 3 mg dosing arm of cohort 2 and three patients in cohort 3. Furthermore, 58% and 50% of patients achieved NAS improvements of two points or greater (with at least one-point reduction in lobular inflammation or hepatocellular ballooning) in the 3 mg dosing arm of cohort 2 and the 1 mg dosing arm of cohort 3, respectively. We anticipate that an increased proportion of patients could achieve resolution of NASH over a longer treatment duration beyond 12 weeks. In conjunction with the fibrosis improvement described above, these data support the notion that aldafermin, as a single agent, has the potential to improve NASH and fibrosis to a larger degree and in a shorter period of time than other investigative agents have demonstrated to date.



Aldafermin Phase 2 Clinical Trial in NASH Patients: Cohort 4 Results

In a double-blind, placebo-controlled cohort of the Phase 2 clinical trial (Cohort 4), 78 biopsy-confirmed NASH patients with F2 and F3 liver fibrosis were enrolled and treated with placebo (n=25) or aldafermin (n=53) for a duration of 24 weeks. The primary endpoint was the treatment effect on absolute changes in LFC as measured by MRI-PDFF compared to placebo. Secondary and exploratory endpoints include relative changes in LFC, biomarkers of liver function and effect on liver histology.

Preliminary topline results indicate that aldafermin achieved its primary endpoint, demonstrating a statistically significant absolute least square (LS) mean reduction in LFC of 8% and a statistically significant LS mean relative reduction in LFC of 39% in the treatment arm, as compared to reductions of 3% and 13%, respectively, in the placebo arm. A statistically significant proportion of patients (68%) treated with aldafermin achieved a ≥5% absolute reduction in LFC compared to placebo (24%). Similarly, a statistically significant proportion of patients treated with aldafermin (66%) achieved a ≥30% relative reduction in LFC compared to placebo (29%). Statistically significant improvements were also observed in the aldafermin treatment arm versus placebo related to biomarkers of liver inflammation and injury (ALT and AST) and PRO-C3. The reductions in key biomarkers to near normal levels were observed as early as week 2 and sustained through week 24, demonstrating that the significant reductions achieved previously at week 12 were durable throughout the treatment period.

Patient liver biopsies were performed at baseline screening and at the end of 24 weeks of treatment and were read using the NASH CRN criteria by one central, independent hepatopathologist who was blinded to patient and treatment assignment. As per protocol, liver biopsy data were analyzed using the “liver histologic population," which was defined as the subset of enrolled patients who had valid, non-missing biopsy data at both baseline and week 24 (n=72). Six patients (three in the aldafermin arm and three in the placebo arm) withdrew prior to the week 24 biopsy for reasons not due to adverse events related to treatment.

The histology results, summarized in the table below, revealed that treatment with aldafermin led to clinically meaningful improvements at 24 weeks versus placebo in fibrosis and in resolution of NASH. Treatment with aldafermin 1 mg resulted in a fibrosis improvement of ≥1 stage with no worsening of NASH in 38% of patients compared to 18% in the placebo arm. 24% of patients in the aldafermin treatment arm achieved the endpoint of resolution of NASH with no worsening of liver fibrosis as compared to 9% of placebo patients. Of note, 22% of patients in the aldafermin treatment arm versus 0% in the placebo arm achieved the composite endpoint of both fibrosis improvement and resolution of NASH, which was statistically significant. Draft guidance by the FDA indicates that each of these is an acceptable endpoint for potential accelerated approval in a future pivotal trial.

Summary of Cohort 4 Preliminary Histology Data[1]		
Proportion of Patients Achieving Endpoints	**Aldafermin 1 mg (n=50)**	**Placebo (n=22)**
Fibrosis improvement (≥1 stage) with no worsening of NASH[2]	**38%**	**18%**
Resolution of NASH with no worsening of liver fibrosis[3]	**24%**	**9%**
Fibrosis improvement and resolution of NASH[4]	**22%***	**0%**
NAS reduction of ≥2 points with no worsening of liver fibrosis	**62%*****	**9%**

** p < 0.05; *** p < 0.0001*

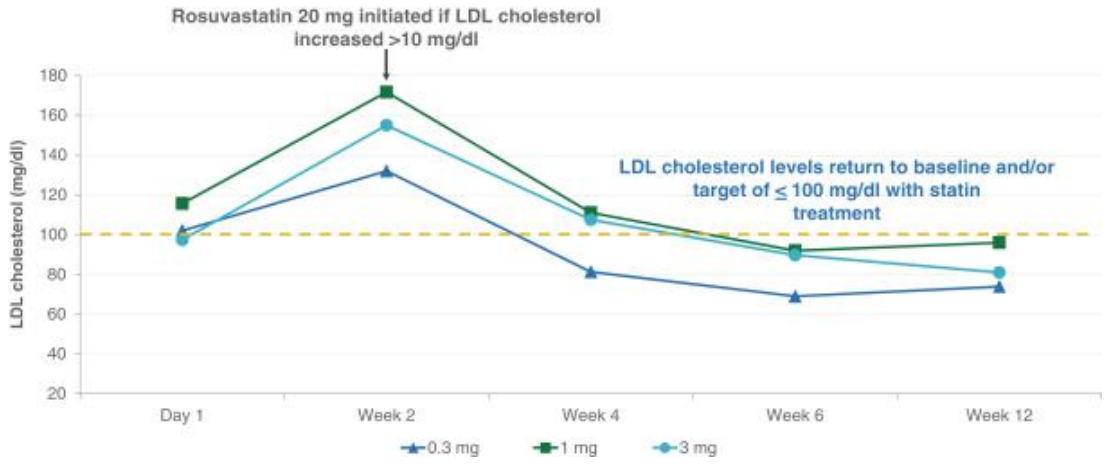
1. Per protocol, analyzed using the "liver histologic population," defined as the subset of enrolled patients who had valid, non-missing biopsy data at both baseline and week 24 (n=72)
2. Defined as patients having an improvement in liver fibrosis ≥1 stage and having no worsening of hepatocellular ballooning, no worsening of lobular inflammation and no worsening of steatosis from baseline to week 24
3. Defined as patients having a NAS of 0 or 1 for lobular inflammation and 0 for hepatocellular ballooning, with no worsening of fibrosis (no progression of NASH CRN fibrosis stage) from baseline to week 24
4. Defined as patients having an improvement in liver fibrosis ≥1 stage with no worsening of NASH and having a NAS of 0 or 1 for lobular inflammation and 0 for hepatocellular ballooning with no worsening of fibrosis, at week 24

Aldafermin Increases in Serum Levels of LDL Cholesterol in NASH Patients

A byproduct of aldafermin's potent inhibition of the classical bile acid synthesis pathway is the elevation of LDL cholesterol in the serum. Cholesterol serves as the precursor molecule in a multi-step enzymatic pathway that generates various forms of bile acids. CYP7A1 is the rate-limiting enzyme in this pathway and, therefore, serves as a regulatory control point for the primary pathway for bile acid synthesis, also known as the classical pathway. Notably, there is an alternative pathway for bile acid synthesis that is not regulated by CYP7A1 activity and produces a subset of the bile acid pool that is believed to produce less caustic varieties of bile. We believe a primary role of FGF19 and aldafermin is to inhibit bile acid synthesis through the classical pathway by activating a signaling cascade that shuts down CYP7A1 activity. As a direct effect of this on-target activity, cellular cholesterol is no longer metabolized to bile acids and is instead shunted into the blood stream, causing an elevation of serum LDL cholesterol. We did not observe the same magnitude of LDL cholesterol elevations with aldafermin in trials we conducted in cholestatic disease patients, such as PBC and PSC.

We believe elevated serum LDL cholesterol is a confirmatory indication of aldafermin and FGF19 activity in NASH patients, which correlates with its beneficial effects on liver health. The impact of these drug-induced changes in cholesterol are unknown. Sustained LDL cholesterol elevations in untreated patients, however, are associated with cardiovascular disease through atherosclerotic plaque development. Through both preclinical studies in cynomologous monkeys and in cohorts 2, 3 and 4 of our Phase 2 clinical trial, we have demonstrated the ability of concomitant statin use to mitigate the serum LDL cholesterol elevations driven by aldafermin activity. The figure below illustrates the mean LDL cholesterol levels over time for patients in cohort 2. Per protocol, the patients' LDL cholesterol levels were measured at baseline and then re-measured after two weeks of aldafermin treatment. If an elevation of LDL cholesterol of at least 10 mg/dl was recorded, patients were directed to take 20 mg of rosuvastatin daily for the remainder of the trial. Nearly all of the treated patients required statin use in cohorts 2, 3 and 4. Where required, patients were elevated to 40 mg rosuvastatin to adequately control their LDL cholesterol while on treatment. Notably, approximately 80% of cohort 2, 87% of cohort 3 and 68% of Cohort 4 at enrollment were not previously receiving statin treatment and, on average, the cohorts had baseline LDL cholesterol levels at or above recommended levels recommended by the American Association of Clinical Endocrinologists and the

European Society of Cardiology/European Atherosclerotic Society, suggesting a statin would already be prescribed as standard of care. For each dose level in cohorts 2, 3 and 4, concomitant statin use mitigated the drug-induced LDL cholesterol rise indicative of CYP7A1 suppression and, in many cases, brought patients below their baseline levels. Additionally, we have investigated the composition of the drug-induced LDL cholesterol particles. This analysis indicated that the aldafermin-induced serum LDL cholesterol manifests as large and potentially less atherogenic lipoproteins, as opposed to the small dense lipoparticles that are thought to be more atherogenic. We believe concomitant statin use, along with aldafermin's triglyceride lowering and high density lipoprotein ("HDL") cholesterol elevating properties, will provide an overall neutral to positive impact on patients' cardiovascular health.



Aldafermin Phase 2 Clinical Trial in NASH: Safety and Tolerability Profile

The most common adverse events in the cohorts 1-3 included increased stool frequency, loose stools, nausea and injection site erythema, with the majority being Grade 1 (mild). A consistent tolerability observation across cohorts 1-3 has been dose-dependent gastrointestinal ("GI") adverse events that manifest in both the upper and lower GI tract. We conducted a Phase 1b trial in patients with chronic constipation and determined that aldafermin has a pro-kinetic effect on the GI tract, which means the increase in stool frequency is caused by greater GI motility and is not related to elevated fecal fat or elevated bile acid content. These results have helped inform mitigation protocols to help patients lessen these GI side effects. This was evidenced in Cohort 4, where the most common adverse events in either treatment arm (diarrhea, headache, abdominal distension, nausea, fatigue, diabetes mellitus and peripheral edema) were primarily mild to moderate and occurred with comparable frequency in both the aldafermin and placebo arms.

A single serious adverse event of acute pancreatitis was reported in cohort 1 and assessed as possibly related to study drug. A total of seven serious adverse events (pleurisy, vertigo, headache, hypertension, cardiac arrest, chest pain and pneumonia), none of which were considered related to study drug, were reported in five subjects in cohort 2. One serious adverse event (kidney mass) was reported in cohort 3 and was not considered related to study drug. In Cohort 4, none of the reported serious adverse events (two in the aldafermin arm and three in the placebo arm) were deemed related to treatment by the clinical site investigator. Preliminary data indicates that there were no tolerability signals identified in this population.

Aldafermin Phase 2b Clinical Trial in NASH – ALPINE 2/3

The ALPINE 2/3 clinical trial is evaluating three dose levels of aldafermin in NASH patients with F2 and F3 liver fibrosis. The ALPINE 2/3 clinical trial is a multi-center, double-blind, placebo-controlled study administering 0.3 mg, 1 mg or 3 mg of aldafermin or placebo, once-daily, subcutaneously for 24 weeks. We expect to enroll a total of approximately 150 patients across 30 sites in the United States. Patients receive liver biopsies to qualify for the trial and at the end of the 24-week treatment. The primary objective of this 24-week trial is to measure the treatment effect of various dose levels of aldafermin on liver histology according to preliminary FDA recommended Phase 3 endpoints of resolution of NASH with no worsening of fibrosis, and fibrosis improvement with no worsening of NASH, as defined above. The enrollment criteria, study design and study conduct are consistent with the FDA draft industry guidance regarding the development of drugs for NASH that was published in December 2018. We plan to report topline results from our ALPINE 2/3 clinical trial in the first half of 2021.

Aldafermin Phase 2b Clinical Trial in NASH – ALPINE 4

The ALPINE 4 clinical trial is designed to evaluate the treatment effect of aldafermin in a population of NASH patients with well-compensated cirrhosis. The objective of this trial is to evaluate whether the fibrosis regression we have observed in patients with F2 and F3 fibrosis can also be achieved in compensated cirrhotic NASH patients, for which liver mortality rates are high and liver transplant is the only option. We plan to initiate the ALPINE 4 clinical trial in the first half of 2020 and expect to enroll approximately 150 patients across 70 sites in the United States, Europe, Hong Kong and Australia. The population of compensated cirrhotic NASH patients in the United States and EU is expected to reach 4.9 million in 2030.

Aldafermin Future Clinical Development Plans

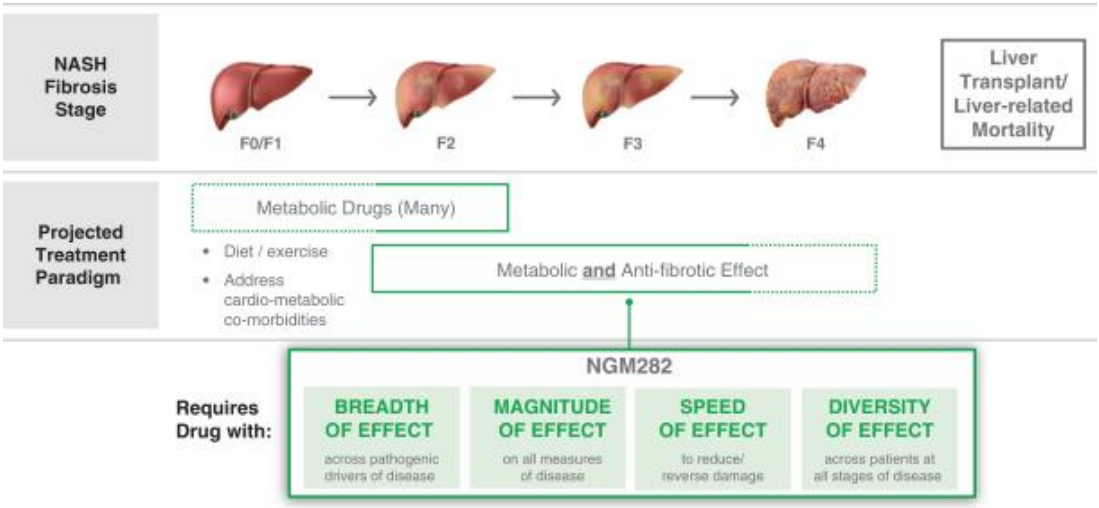
Our development strategy is to leverage the results of our completed 24-week double-blind, placebo-controlled Cohort 4 of our Phase 2 clinical trial to inform early Phase 3 planning and design. We expect that ALPINE 2/3 clinical trial results in the first half of 2021 will provide further information to support a pivotal, single dose level, Phase 3 program to enable a biologics license application (“BLA”) filing.

We believe the totality of the data produced by these Phase 2 clinical trials will provide insights required to appropriately design Phase 3 clinical trials required for drug approval and optimally position the therapeutic in the market.

Future Commercial Positioning of Aldafermin as a Therapeutic in the NASH Market

We believe the clinical data produced with aldafermin in NASH patients to date suggests a potential drug profile that is unique in the current landscape of NASH therapeutics in development. Our preliminary data suggests aldafermin is capable of improving fibrosis in patients as early as 12 weeks of treatment, while also exerting a positive impact on the other parameters of NASH, including steatosis, lobular inflammation and hepatocellular ballooning.

If our initial signals of activity continue in later-stage clinical development, we believe that aldafermin, as a once-daily injectable medication, will be well suited to treat NASH patients with F2, F3 and, potentially, early F4 fibrosis. Together, these target patient populations were believed to encompass approximately 6.7 million patients in the United States in 2015, and are expected to grow to 14.1 million by 2030. As diagrammed below, our goal is to position aldafermin, if approved, to physicians as a potent, rapidly-acting medication that can repair NASH-damaged livers to avoid progression to end-stage liver disease and liver transplantation. This advanced disease population is typically under the care of hepatologists, as contrasted with the typically asymptomatic early-stage NASH population, the majority of whom have not yet been diagnosed. We expect other agents in development, many of which are delivered orally, will serve a complementary role in the treatment of earlier-stage disease or may ultimately require combination treatment with other mechanisms to have an improved effect over its single-agent activity.



Commercial Product Development and Life-cycle Management

In clinical trials to date, aldafermin has been delivered using a pre-filled single-use glass syringe. We are seeking to develop a formulation of the agent to enable testing a more commercially-attractive multi-use pen injector, similar to the devices currently delivering injectable type 2 diabetes treatments. We expect that the multi-dose pen format could be available for product launch, if aldafermin is approved. Our objective is to present a multi-dose pen with needle gauge 29 or smaller, which will be familiar to the large number of NASH patients with type 2 diabetes who also require injections of insulin or GLP-1 products.

Longer term, we are pursuing a life-cycle management strategy to develop a longer half-life version of aldafermin that will require less frequent dosing. At present, we have programs investigating delayed-release technologies and protein modification to support this strategy. These efforts are currently at the research stage.

Early Aldafermin Clinical Development and Preclinical Development

Our development program for aldafermin in NASH has been informed by several precursor and parallel clinical studies, as well as preclinical findings in a variety of NASH animal models. In all clinical trials, aldafermin had an acceptable tolerability profile. A summary of the studies conducted with aldafermin are listed below:

Aldafermin Phase 1 Clinical Trial

We conducted a Phase 1 randomized, double-blind, placebo-controlled, single ascending dose (“SAD’) and multiple ascending dose (“MAD”), study to evaluate the safety, tolerability and pharmacokinetics of aldafermin in healthy adult participants.

In this blinded, placebo-controlled, Phase 1 clinical trial, 119 overweight or obese but otherwise healthy adults were randomized to receive aldafermin or placebo as a daily subcutaneous injection in escalating doses. In both the SAD and MAD trials, aldafermin was well tolerated and exhibited approximately linear pharmacokinetics with no immunogenicity. There were no serious adverse events. The most frequently observed adverse events were diarrhea, vomiting, nausea and injection site reactions. Also, there were no laboratory changes in aldafermin-treated subjects that would indicate an abnormality in any organ system, as determined by the Safety Data Monitoring Committee for the study, nor were anti-drug antibodies observed.

Aldafermin Phase 2a Clinical Trial (Type 2 Diabetes)

We conducted a 28-day, randomized, double-blind, multi-center trial to evaluate aldafermin in subjects with type 2 diabetes that were inadequately controlled by metformin. As a consequence of the contribution of obesity and insulin resistance to both conditions, there is a substantial overlap in the prevalence of type 2 diabetes and NASH patients. The type 2 diabetes trial was also designed to measure several of the metabolic parameters that are believed to play a role in the disease progression of NAFLD and NASH, including indicators of insulin sensitivity, triglyceride levels and enzyme levels of liver transaminases, such as ALT and AST. Three doses of aldafermin were tested to assess changes from baseline in biochemical markers associated with type 2 diabetes, such as fasting plasma glucose and stimulated glucose/insulin.

The primary endpoint measured by this trial was the change in fasting plasma glucose after 28 days of treatment. Although this endpoint was not different in the aldafermin subjects as compared to the control arm, there were trends towards improvement in insulin sensitivity, as measured by Homeostatic Model Assessment of Insulin Resistance (“HOMA-IR”), and a statistically significant weight loss observed in the 10 mg group, which lost an average of 2.6 kilograms over the 28 days of treatment ($p<0.05$). Moreover, there was a statistically significant reduction in triglyceride concentrations with the 2 mg ($p<0.001$) and 10 mg ($p<0.001$) doses, and dose-dependent reductions in ALT and AST levels, consistent with improvements in liver health. However, as this trial did not meet its primary endpoint, we decided not to pursue development of aldafermin in type 2 diabetes. The trial did establish that aldafermin demonstrated improvements in both metabolic and liver health in a patient population that closely resembles NASH patients.

Overall, aldafermin was well tolerated at each dose. There were no serious adverse events reported, though nine subjects withdrew due to adverse events. The most frequently observed adverse events were GI side effects, which were primarily loose stools/diarrhea, nausea and injection site reactions. One subject developed antibodies against aldafermin that appear to cross-react with FGF19. This subject did not demonstrate any biochemical or clinical safety concerns while in the study, and we have not identified any safety concerns while monitoring the subject following the study.

Aldafermin Phase 2 Clinical Trials in Cholestatic Diseases: PBC and PSC

We conducted an exploratory Phase 2a clinical trial in PBC patients testing daily subcutaneous injections of aldafermin for 28 days, and followed it with a 52-week extension study to assess longer-term safety and tolerability of daily aldafermin. While both doses tested in the 28-day study met the primary endpoint of a statistically significant reduction in ALP levels (a validated surrogate endpoint by the FDA), we determined that, with two oral alternatives on the market with similar efficacy, the indication was not well-suited for aldafermin. Aldafermin was well tolerated at each dose and showed no evidence of drug-induced pruritus. The majority of adverse events were mild or moderate. A statistically significant elevation of LDL cholesterol concentration was not observed in this patient population.

We also conducted an exploratory Phase 2 clinical trial in PSC patients with aldafermin. Unlike PBC, there are currently no approved medications for PSC and, similarly, there are no validated clinical endpoints accepted by the FDA for approval. Aldafermin did not achieve the primary endpoint in the study, which was a statistically significant reduction in ALP levels at the end of treatment. While ALP concentration has also been viewed as a possible surrogate endpoint in PSC, the correlation with disease progression is not as clear as in PBC, and the FDA is developing guidance to drug developers as to an acceptable path to approval. We do not intend to further develop aldafermin in PSC until a development path is more specifically defined in the indication. However, the results of the study also provide utility in understanding the mechanism of aldafermin across the diseases tested. Notably, PRO-C3 and ELF levels, which are markers of fibrosis, improved significantly in the treatment group, suggesting that aldafermin may also have a direct impact on fibrosis that is independent from its metabolic activity, as the PSC patient population does not have elevated LFC. Furthermore, a statistically significant elevation of LDL cholesterol concentration was not observed in this patient population.

Aldafermin Phase 1 Clinical Trial in GI Motility

A consistent finding in our Phase 2 clinical trials has been an association of aldafermin to dose-related abdominal cramping and increased stool frequency. To further investigate and characterize these GI effects, we conducted a randomized, placebo-controlled, 14-day study in patients with functional constipation that tested two doses of aldafermin, 1 mg once-daily and 6 mg once-daily. The objective of the study was to evaluate the effects of aldafermin on colonic transit, stool frequency and consistency, hepatic bile acid synthesis, fecal fat and bile acid levels. Thirty-one patients with functional constipation were randomized on a 1:1:1 basis to placebo (n=10), 1 mg aldafermin (n=10) and 6 mg aldafermin (n=11) arm. Overall, aldafermin altered bowel function in this group of chronic constipation subjects through increased frequency of bowel movements, looser stool form and increased ease of passage, and significantly accelerated gastric and colonic transit. There were no significant differences in fecal fat or weight between the placebo and treatment groups, suggesting that GI effects of aldafermin are not secondary to an increase in fecal fat. We believe the results of this study show that GI side effects are primarily due to increased colonic motility, rather than increased small bowel or colonic secretion, the latter of which is more characteristic of diarrhea than loose stools. We have applied this mechanistic understanding to our clinical trial by suggesting that subjects time their dosing around meals and moderate the size of a meal in proximity to dose. While the GI side effects of aldafermin are consistent through the clinical studies conducted to date, we have observed that those patients on 3 mg and lower doses that do experience GI side effects generally report mild to moderate effects that resolve on treatment and do not lead to discontinuation of the drug.

Aldafermin Engineered to Create a Non-tumorigenic Form of FGF19

Human FGF19 is only about 50% identical to its mouse ortholog, known as FGF15. *In vivo* studies have shown that transgenic mice expressing the human FGF19 hormone at greater levels than levels expressed in healthy humans develop hepatocellular carcinoma (“HCC”). Aldafermin is a variant of FGF19, engineered to remove the tumorigenic properties of human FGF19 in mice while retaining its beneficial effects. Prior to designating aldafermin for development, we carried out an extensive *in vivo* analysis of the structure-function relationship to define the domains in FGF19 responsible for its various activities. Our goal was to identify a variant of human FGF19 that was non-tumorigenic in mice but that retained maximal activity against both the FGFR1c/KLB and FGFR4/KLB receptor complexes so that full metabolic and bile acid effects would be maintained. We designed and evaluated over 150 FGF19 variants to identify compounds with the desired profile. Aldafermin is approximately 95% identical to the naturally-occurring human FGF19, with three amino acid substitutions and a five-amino acid deletion from the amino terminus.

Aldafermin retains the metabolic activity of FGF19 through the FGFR1c/KLB receptor complex and the bile acid activity of FGF19 through the FGFR4/KLB receptor complex. Importantly, aldafermin is a biased ligand of FGFR4, meaning that it selectively activates signaling through the FGFR4/KLB receptor complex in a manner that retains beneficial activity on bile acid production but does not cause HCC in mice, as shown in three different models of oncogenic potential. Furthermore, co-administration of aldafermin and FGF19 *via* gene delivery in a *db/db* mouse model eliminated the expected FGF19-driven HCC, suggesting that aldafermin blocked the ability of FGF19 to occupy the relevant receptor and signal in such a way as to cause HCC. We have also explored the biological mechanism that drives the FGF19 oncogenic signal in mice and have determined that the interleukin-6 (“IL-6”)/STAT3 axis is essential for the activity. The elements of the IL-6/STAT3 axis that drive the FGF19 oncogenic signal in mice are not activated with aldafermin.

NGM313: An Insulin Sensitizer for the Treatment of Type 2 Diabetes and NASH

NGM313, also known as MK-3655, is a proprietary, agonistic antibody selectively activating FGFR1c/KLB that we believe has the potential to be a once-monthly injectable insulin sensitizer for the treatment of NASH and type 2 diabetes. In November 2018, Merck exercised its option for a license to further research, develop and commercialize NGM313 and other FGFR1c/KLB agonists pursuant to our Collaboration Agreement. In Phase 1 clinical testing, NGM313 has demonstrated favorable tolerability and preliminary data has shown the agent is capable of reducing LFC and improving metabolic biomarkers in obese insulin resistant subjects with NAFLD after a single dose. We believe that NGM313 has the potential to be a treatment for those patients with NASH with early to moderate fibrosis with or without type 2 diabetes.

Type 2 Diabetes

Type 2 diabetes is a common co-morbidity of obesity and NAFLD, and a disease in which the concentration of blood sugar is elevated due to an imbalance of insulin production from insulin secreting beta cells in the pancreas and insulin action at the tissue level, known as insulin resistance, causing damage to small and large blood vessels and, potentially, leading to blindness, amputation and kidney disease along with an increased risk of heart attack, stroke and premature death. In type 2 diabetes, the body's tissues become resistant to the effects of insulin over time, requiring the pancreas to produce an unsustainably large amount of insulin to compensate. The growing epidemic of obesity is driving an increasing number of diabetes sufferers, as there is a close relationship between increasing BMI and the relative risk of developing type 2 diabetes.

According to the Centers for Disease Control and Prevention in 2015, an estimated 30 million people in the United States had diabetes, with 1.5 million new cases being added every year. Over 80 million people in the United States are pre-diabetic, the majority of whom are expected to become diabetic in the next ten years. The medical costs of treating the diabetic patient population in the United States alone are believed to have been $327 billion in 2017. Given the large patient population and high unmet need, pharmaceutical companies have developed multiple classes of therapies. The most recent classes include GLP-1 analogs, sodium-glucose cotransporter 2 ("SGLT2") inhibitors and dipeptidyl peptidase IV ("DPP-IV") inhibitors.

The currently available types of treatments include:

- various forms of insulin replacement therapies and agents to stimulate insulin secretion, whereby the insulin levels are boosted to help decrease blood glucose levels, including recombinant insulin, sulfonylureas and meglitinides;

- agents that inhibit the absorption of glucose in the gut, increase the excretion of glucose in the kidney and/or decrease the production of glucose in the liver, thereby reducing blood glucose levels, including alpha-glucosidase inhibitors, SGLT2 inhibitors and biguanides, like metformin;

- drugs that produce a combination of insulin boosting and glucose absorption-inhibiting activity, including incretins, such as GLP-1 analogs and DPP-IV inhibitors; and

- drugs that increase the body's sensitivity to insulin, thereby making the insulin present in the blood have a more potent effect on lowering blood glucose, which currently consists of thiazolidinediones ("TZDs").

The majority of patients with type 2 diabetes are insulin resistant and have associated metabolic dysregulation caused by lipid abnormalities, fatty liver, hypertension and chronic vascular inflammation. Insulin resistance and beta cell dysfunction are interrelated pathogenic states that lead to persistent hyperglycemia and development of type 2 diabetes. Insulin resistance results from defective insulin signaling in glucose recipient tissues and the persistent elevation of glucose concentrations above the physiological range, leading to increased insulin demand. Beta cell dysfunction, resulting from inadequate glucose sensing to stimulate insulin secretion, is compounded by insulin resistance and also induces hyperglycemia in patients with type 2 diabetes. Preserving beta cell function and insulin signaling in type 2 diabetes patients remain an unmet medical need as persistent hyperglycemia leads to continued progression of diabetes. Even with the multiple classes of diabetes drugs available, only about one-half of patients with diabetes achieve their glycemic goal.

Insulin Sensitizers for the Treatment of Type 2 Diabetes

Insulin resistant patients that remain inadequately controlled often have NAFLD, low HDL cholesterol level and increased waist circumference, and are likely the best candidates for treatment with insulin sensitizers. TZDs, such as pioglitazone and rosiglitazone, are a notable class of drugs that function as insulin sensitizers to potentiate the effect of insulin, improving glycemic control and dyslipidemia and, therefore, providing a valuable addition to diabetes therapy. As a monotherapy, pioglitazone improves the sensitivity of hepatic and peripheral tissue to insulin, increases insulin-dependent glucose disposal, enhances cellular responsiveness to insulin and, thus, improves dysfunction in glucose homeostasis. This decreased insulin resistance results in a durable lowering of blood glucose, insulin and hemoglobin A1c ("HbA1c") levels. However, the clinical use of TZDs has been limited by the risk of adverse events, including congestive heart failure, for which there is a FDA boxed warning, weight gain, peripheral edema/fluid retention, bone fractures and, for pioglitazone, an association with bladder cancer.

We believe the introduction of an insulin sensitizer without the adverse effects and safety profile of the TZDs would provide a meaningful addition as combination therapy with incretins, with the goal of normalizing glucose levels in patients with type 2 diabetes. While numerous new drug classes are available, none target insulin resistance nor have the potential to resolve persistent hyperglycemia when used in combination with other available diabetes treatments.

Insulin Sensitizers for the Treatment of NASH

Insulin resistance has been implicated as a key condition leading to hepatic steatosis and, subsequently, NASH. Activation of the immune system contributes to the development of insulin resistant adipocytes that release excessive amounts of free fatty acids and cause insulin resistance and lipoapoptosis in peripheral tissues, including the liver, muscle and pancreatic beta cells. Increased hepatic triglyceride synthesis and accumulation of triglyceride-derived toxic lipid metabolites activates intracellular inflammatory pathways within hepatocytes, Kupffer and other immune cells. The subsequent activation of hepatic stellate cells leads to collagen deposition, fibrosis development and, eventually, cirrhosis of the liver. Treatments that can rescue the liver from lipotoxicity, in particular the effects of free fatty acids, by restoring peripheral tissue insulin sensitivity and/or preventing activation of inflammatory pathways and oxidative stress, hold promise for the treatment of NASH.

An estimated 65% of type 2 diabetes patients have NASH. The presence of diabetes is associated with worse liver disease and, in patients with NAFLD and NASH, type 2 diabetes is associated with more severe hepatic and adipose tissue insulin resistance, and more advanced liver steatosis, inflammation and fibrosis by liver histology. In addition, administration of insulin may increase steatosis, making the treatment of patients with type 2 diabetes and NASH challenging.

The role of insulin resistance and hyperglycemia in the pathogenesis of NAFLD suggests that improving insulin sensitivity and normalizing glucose levels could prevent the development of NASH and progression of disease. It is inconclusive whether current drugs for the treatment of diabetes, such as metformin, DPP-IV inhibitors, SGLT2 inhibitors and GLP-1 agonists, are effective for the treatment of NASH and, for some, if histological benefit is observed, it is unclear whether the effect is related to the concomitant weight loss with treatment. Proof-of-concept studies with an insulin sensitizer, pioglitazone, whose main target at the molecular level is PPAR-gamma in adipose tissue, have shown that treatment after six months, as compared to placebo, resulted in statistically significant improvements in histological findings associated with NASH, with reductions in steatosis, hepatocellular ballooning and lobular inflammation. Fibrosis scores improved significantly relative to baseline in the pioglitazone group, however, the change from baseline did not differ significantly between the placebo and pioglitazone groups after six months of treatment. Pioglitazone treatment increased hepatic insulin sensitivity and glucose clearance, which led to significant reductions in plasma free fatty acids, glucose and insulin levels in NASH patients.

With approximately 17.5 million patients in the United States with type 2 diabetes and NASH, there exists a substantial unmet medical need for a single treatment that addresses pathophysiological states common to both diseases, including insulin resistance, lipid metabolism dysfunction and increased lipotoxicity at the level of the liver. To date, of the FDA approved anti-diabetes drugs on the market, only pioglitazone and liraglutide have demonstrated a benefit on components of the NAS in controlled studies on patients with NASH. We believe NGM313 has the potential as an insulin sensitizer for use as monotherapy or in combination with other drug classes, like GLP-1 analogs, to halt the progression of, and potentially reverse, diabetes and NASH.

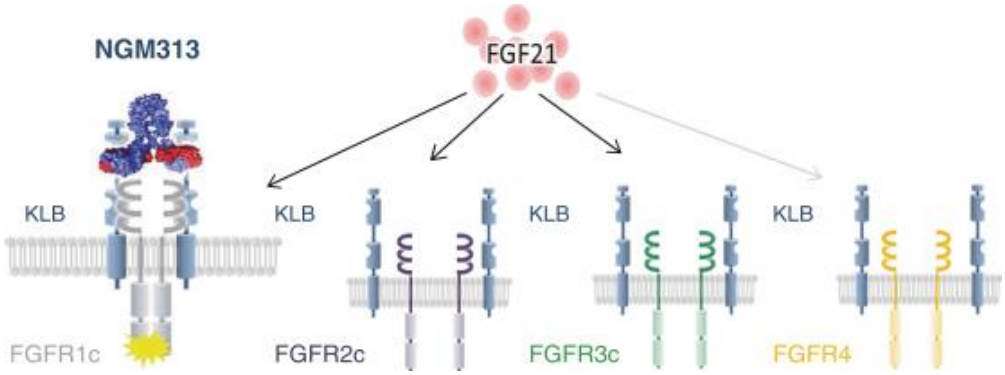
NGM313 Mechanism of Action

NGM313 is a humanized monoclonal agonistic antibody, with the potential for once-monthly dosing, that binds to a unique epitope of KLB, resulting in the selective activation of FGFR1c and signaling through the metabolic pathway utilized by FGF21-based ligand therapies. FGF21 is a protein hormone that is secreted by the liver, adipocytes, pancreas and skeletal muscle. In animal testing, FGF21 plays a role in fasting and starvation by acting on adipose, or fat, cells to increase energy expenditure by stimulating glucose uptake. Notably, the effect of FGF21 on glucose uptake is additive to, but not synergistic with, insulin. Unlike insulin, the response of fat cells to FGF21 requires prolonged exposure to this hormone. Moreover, FGF21 acts to lower plasma triglyceride levels over an extended period. FGF21 also protects animals from diet-induced obesity when overexpressed in transgenic mice and lowers blood glucose and triglyceride levels when administered to diabetic rodents.

FGF21 exerts its effects on metabolic processes by signaling through the receptors known as FGFR1c, FGFR2c and FGFR3c, but not the receptor known as FGFR4. KLB functions as a co-receptor to enhance the binding of these receptors and is essential for mediating FGF21 activity. FGF receptors are expressed on cells in many tissue types, but KLB is mainly expressed in fat cells and other tissues, such as the pancreas and liver.

FGF21-based therapeutics have generated interest in the pharmaceutical research and development community because they represent a novel approach to treating multiple aspects of the metabolic syndrome; however, attempts by other companies to translate FGF21 into a product with clinical application have had limited success. While native FGF21 is thought to have limitations for drug development, including potential effects on cortisol, bone and blood pressure, various animal studies have demonstrated that modified FGF21 ligands simultaneously regulate insulin sensitivity and blood glucose and increase energy expenditure, fat utilization and lipid excretion. Multiple pharmaceutical companies have conducted human testing of therapeutics regulating the FGF21 pathway. Administration of modified FGF21 ligands to humans results in variable improvement in insulin sensitivity, reduction in LFC and improvement in lipid profile and body weight loss, suggesting potential utility in treating obesity, type 2 diabetes, dyslipidemia and NASH. However, the blood glucose reductions observed in humans following dosing with modified FGF21 ligands, to date, have not been meaningful. It is thought that these FGF21-based protein therapeutics have produced inadequate glucose reductions due to a shorter than optimal half-life or counter-regulatory mechanisms triggered from activity across multiple receptor types. It has been postulated that a therapeutic regulating the FGF21 pathway with an extended half-life might improve its efficacy profile for type 2 diabetes. Furthermore, while an FGF21-based agent has demonstrated significant reductions in liver steatosis and non-invasive markers of disease in NASH subjects, the effect of FGF21 on liver histology in NASH patients has not been assessed to date.

NGM313, an Agonistic Antibody of the FGFR1c/KLB Receptor Complex



We believe that developing a specific, agonistic antibody that selectively activates the FGFR1c/KLB pathway would obviate the risks associated with therapeutics based on the native FGF21 ligand. The development candidate, NGM313, exhibits highly specific binding with KLB, resulting exclusively in the activation of FGFR1c-mediated signaling; it does not trigger signaling through other FGF receptors, such as FGFR2c, FGFR3c or FGFR4. Moreover, as NGM313 recognizes an epitope on KLB that is distinct from the FGF19 or FGF21 binding sites, it does not compete with these natural ligands for binding with the FGFR1c/KLB complex. We believe that this non-overlapping binding site reduces the potential for side effects resulting from NGM313 inhibition of endogenous FGF19 and FGF21 hormone activity.

NGM313 Phase 1b Early Proof-of-Concept Clinical Trial

We conducted a Phase 1b randomized, open-label, parallel group trial to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of a single NGM313 dose or daily oral pioglitazone in 25 obese insulin resistant subjects with NAFLD. The Phase 1b clinical trial evaluated the ability of NGM313 to decrease LFC to support the clinical development of NGM313 in NASH, as well as its effect on glucose disposal to assess the potential of NGM313 in the treatment of patients with type 2 diabetes. A single subcutaneous dose of 240 mg NGM313 was selected based on the clinical pharmacokinetic and pharmacodynamic data, and the tolerability profile from the Phase 1 SAD/MAD trial described below. Pioglitazone was chosen as a positive control in this study as it is the only agent approved for clinical use as an insulin sensitizer for the treatment of type 2 diabetes and also has demonstrated beneficial activity in NASH patients. The highest approved daily oral dose of 45 mg pioglitazone was used in this study to provide the opportunity for maximal efficacy as a comparator in a trial with a short treatment duration of five weeks.

The primary objectives of the study were to evaluate changes from baseline in LFC as measured by MRI-PDFF at day 36 and changes from baseline in whole body insulin sensitivity at day 29 in subjects treated with NGM313 as compared to pioglitazone. A single dose of NGM313 resulted in a statistically significant least squares mean change from baseline to day 36 of -6.3% and -37% in absolute and relative LFC, respectively ($p<0.0001$), while daily dosing of 45 mg pioglitazone resulted in a statistically significant least squares mean change from baseline to day 36 of -4.0% and -25%, respectively ($p<0.001$). The change from baseline with NGM313 treatment was not significantly different relative to that observed with pioglitazone ($p=0.08$), however, the study was not powered to demonstrate statistical significance between groups. Historically, a relative reduction of LFC of 29%, as measured by MRI-PDFF, was associated with a histological response of a NAS improvement of two stages or greater. In addition, preliminary results indicated that a single dose of NGM313 resulted in a statistically significant mean decrease from baseline of 0.24% in HbA1c at day 36 ($p<0.0001$), as compared to a decrease of 0.11% with a daily dose of 45 mg of pioglitazone, without hypoglycemia. A reduction in HbA1c of the magnitude observed in this study's insulin resistant, non-diabetic patient population in this time frame supports the promise of NGM313 to potentially improve glucose control in type 2 diabetes patients. This was accompanied by statistically significant reductions from baseline in HOMA-IR (a measure of insulin resistance), serum concentrations of fasting glucose, ALT, AST, triglycerides and LDL cholesterol, and a statistically significant increase in HDL cholesterol levels at day 28 (all $p<0.05$), as summarized in the table below. PRO-C3 was also significantly reduced with NGM313 treatment but not with pioglitazone ($p<0.01$).

NGM313-treated patients had a least squares mean increase from baseline in body weight of 1.6 kg at day 36, as compared to 2.4 kg with pioglitazone. This study indicated that NGM313 was well tolerated, with no serious adverse events and no adverse event leading to study discontinuation. All adverse events observed during the course of the study were deemed mild, with increased appetite (12%) being the only adverse event reported in at least 10% of NGM313-treated subjects.

Data from the Phase 1b clinical trial, in addition to the data described below from the Phase 1 SAD/MAD clinical trial, support the potential for NGM313 to be the first insulin sensitizer for the treatment of NASH and type 2 diabetes, without the safety concerns that plague currently available agents targeting insulin resistance, such as edema, fluid retention, heart failure and bone fractures. Given that the metabolic changes of NGM313 were seen after only a single dose, it is likely that a more substantial improvement would be observed after longer duration of treatment. We expect Merck to initiate a Phase 2b histology study of NGM313 in NASH subjects in the second half of 2020.

NGM313 Phase 1 SAD/MAD Clinical Trial

Our first-in-human Phase 1 clinical trial was a blinded, placebo-controlled study in overweight or obese but otherwise healthy adults in which single and multiple once-monthly subcutaneous injections of NGM313 or placebo were tested to evaluate the safety, tolerability and pharmacokinetics of NGM313. NGM313 was well tolerated, with signs of biological activity indicative of insulin sensitization, after a single dose.

In the MAD portion of the study, three once-monthly doses ranging from 10 mg to 240 mg of NGM313 were administered and, after 12 weeks, mean decreases from baseline in HbA1c, fasting glucose, fasting insulin and HOMA-IR were observed at the higher doses relative to placebo. Similar to the SAD portion of the study, a favorable lipid profile was demonstrated at the end of treatment on day 85, as shown in the table below. An increase in placebo-subtracted body weight at end of treatment of 1.6 kg and 2.4 kg was noted in patients from the SAD and MAD cohorts, respectively, that received the highest dose level of NGM313. This trend in body weight increase is consistent with the degree of insulin sensitization effects observed at these doses, and there was no evidence of edema, fluid retention or hemodilution associated with NGM313 treatment. Despite the change in weight, there was no statistically significant increase in the waist circumference in these cohorts of subjects receiving NGM313. The beneficial changes in glucose metabolism, lipid levels and biomarkers of insulin sensitization supported further evaluation of NGM313 in patients with fatty liver and insulin resistance.

NGM313 Improves Key Glucoregulatory and Lipid Parameters

	Phase 1 SAD (Change from Baseline at Day 29)		Phase 1 MAD (Change from Baseline at Day 85)	
Parameter	**Placebo** (n=19)	**NGM313 240 mg** (n=9)	**Placebo** (n=13)	**NGM313 240 mg** (n=14)
HbA1c (%)	-0.04	-0.18	0.03	-0.11
Fasting Glucose (mg/dl)	2.2	-3.8	-2.3	-4.7
Fasting Insulin (mU/l)	1.6	-4.0	-0.9	-3.9
HOMA-IR	0.5	-1.0	-0.1	-1.0
Triglycerides (mg/dl)	16	-46	10	-50
HDL (mg/dl)	-2	10	0	8
LDL (mg/dl)	-12	-25	-5	-15

In both the SAD and MAD cohorts, NGM313 was well tolerated. There were three serious adverse events reported (adjustment disorder in the placebo group; lower GI hemorrhage and cholecystitis in the NGM313 groups), and they were considered to be unrelated to study drug. The majority of adverse events were mild to moderate in severity, and treatment-related events with the greatest proportion of subjects were GI disorders, injection site reactions, upper respiratory tract infections, headache and increased appetite. In contrast to pioglitazone, where an increased risk of bone fractures in women has been described, there were no changes in bone mineral density and bone formation and resorption markers observed in the MAD trial among subjects treated with NGM313. No symptomatic hypoglycemia was observed with NGM313 treatment. The pharmacokinetic profile suggests that NGM313 displays nonlinear kinetics following a single dose, which is anticipated for an antibody that displays target-mediated clearance. There was some presence of anti-drug antibodies observed, but it did not appear to affect the pharmacokinetics or tolerability profile of NGM313.

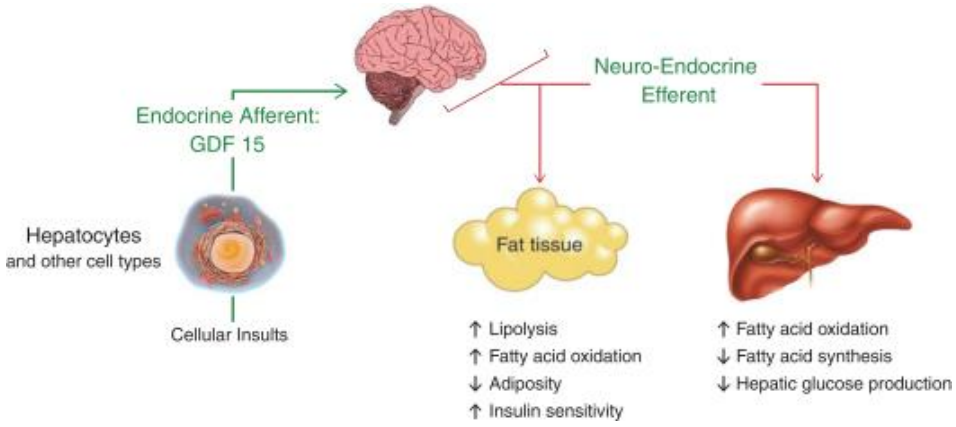
NGM395: Engineered Variant of GDF15 for the Potential Treatment of Metabolic Disease

NGM395 is a proprietary, engineered variant of the hormone GDF15 that has the potential to be a once-weekly or less frequent subcutaneous injection for the treatment of metabolic syndrome. We first discovered that the metabolic activity of GDF15 is mediated by GFRAL, the exclusive, brain stem-restricted receptor for GDF15, in 2013. In 2015, under the Collaboration Agreement, we granted Merck a worldwide license to further research, develop and commercialize our GDF15 receptor agonist program, which includes NGM395 as well as other GDF15 receptor agonists, including a product candidate referred to as NGM386. Merck initiated first-in-human studies of NGM386 in 2016 and completed a Phase 1 MAD clinical trial in 2018. Preliminary data from the study indicated that daily NGM386 treatment for 28 days was generally well tolerated, but did not result in significant body weight loss in obese subjects in this safety study of limited duration. Effective May 31, 2019, Merck terminated its license to the GDF15 receptor agonist program and, upon termination, we regained full rights to the GDF15 receptor agonist program, including both NGM395 and NGM386. Following our assessment of the NGM395 Phase 1 study results, given both the demonstrated tolerability of NGM386 and the more optimal pharmacokinetic properties of NGM395, we chose to suspend development of NGM386 and move NGM395 into clinical development. In the first quarter of 2020, we initiated a Phase 1 SAD clinical trial to determine the safety, tolerability and pharmacokinetics of NGM395 in obese but otherwise healthy adults.

Overview of GDF15 Pathway and Our Discovery of the GDF15 Receptor, GFRAL

GDF15, also known as MIC-1 and NAG-1, is expressed in peripheral tissues relevant to metabolic function. We identified GDF15 in an unbiased screen of putative secretory factors using our rAAV gene delivery approach in diet-induced obese (“DIO”) mice. In this screen, GDF15 produced one of the most potent and efficacious metabolic responses we have observed, effectively normalizing blood glucose and significantly reducing body weight. The effects of GDF15 on food intake, energy expenditure and body weight were known. We discovered that GDF15 causes peripheral lipolysis, which is the burning of fats to create free fatty acids as a source of energy, through the sympathetic nervous system. However, the pharmaceutical industry’s GDF15 drug discovery efforts had been significantly impeded by the lack of understanding regarding the identity of its cognate receptor and signaling pathways. We identified GFRAL as the exclusive, brain stem-restricted receptor for GDF15 in 2013 and, in 2017, published a landmark paper in the journal *Nature* describing its discovery and the elucidation of its crystal structure by our scientists.

Our research suggests that GDF15 is elevated in peripheral tissues following cellular insults, such as oxidative, metabolic or hypoxic stress, and may serve as a messenger hormone to communicate with the brain stem and orchestrate adaptive metabolic changes to cope with the energy demand of cells under various stress conditions. Among these adaptations are reduced food intake and a change in the fuel flux that favors the burning of free fatty acids through lipolysis, instead of burning carbohydrates. We discovered that GDF15 acts directly on GFRAL, a receptor located exclusively in the area postrema (“AP”) and nucleus tractus solitarius of the brain stem. The AP is a circumventricular organ that is outside the blood-brain barrier, which means that it can readily sense any changes in the bloodstream. This discovery provided a mechanistic basis for the regulation by GDF15 of whole body metabolism through a distinct neural circuitry.



Elucidating the Biology of GDF15 and GFRAL

We have generated the following results supporting the biological role of GDF15 and its receptor, GFRAL:

- recombinant GDF15 protein was shown to confer potent metabolic benefits upon administration in mouse disease models, including decreased glucose levels without hypoglycemia, improved oral glucose tolerance, decreased insulin levels, increased lipolysis, reduced food intake and body weight loss;

- weight loss and metabolic effects from GDF15 expression in DIO mice were observed even at systemic levels as low as 0.6 ng/ml, a concentration comparable to the endogenous levels of this hormone found in humans;

- a mouse strain in which GFRAL was knocked out was overweight compared to normal mice when fed a high-fat diet. However, the GFRAL receptor knockout mice were non-responsive to treatment with an engineered variant of GDF15 and, unlike their normal counterparts, the animals continued to show elevated body weight and increased food intake. This suggests that GFRAL is the primary receptor through which GDF15 acts to achieve its metabolic effects; and

- vagotomy, a surgical procedure that cuts nerves in the sympathetic nervous system traveling through the vagus nerve, reduces GDF15-induced body weight loss but does not affect GDF15-induced anorexia in mice. This suggests that GDF15 controls body weight through two pathways: a central pathway regulating food intake and a peripheral, vagal-dependent pathway modulating fat utilization.

In addition to the evidence generated in our labs, independent research has reported that GDF15 gene knockout mice weigh more and have increased obesity due to increased spontaneous food intake. Infusion of human recombinant GDF15 that raised serum levels of GDF15 knockout mice to within the normal human range led to reduced body weight and food intake in a dose-dependent fashion.

Engineered Protein Variants of GDF15

We discovered in 2013 that GFRAL was the cognate receptor for GDF15, several years before other pharmaceutical companies became aware of the receptor identity. During this multi-year period we developed novel insights into the mechanism of action of GDF15 and the structure and function of the GDF15/GFRAL interaction. Through high-resolution X-ray crystallography, we discovered that GDF15 crystal structure revealed a hydrophobic region on the protein surface that we believe impairs the solubility and, therefore, the manufacturability of the native hormone. Armed with this structural information and functional assays that we were able to develop through the elucidation of the GDF15 signaling pathway, we conducted a systematic “structure-activity relationship” analysis of GDF15 and GFRAL to identify the critical functional domains of both the hormone and its receptor. With this data, we generated NGM395 and NGM386 as optimized GDF15 variants that exhibit significantly improved pharmaceutical properties. Between 2015 and 2019, Merck was responsible for the development and manufacturing of NGM395 and NGM386.

NGM395 is a long-acting fusion protein variant of GDF15 that has a pharmacokinetic profile suitable for weekly dosing. Three-month studies of NGM395 in two species were completed with no observation of treatment-related changes in organ weight, cell morphology, neurobehavior or clinical pathology that were not attributable to body weight loss.

NGM120: An Antagonistic Antibody Binding GFRAL for the Potential Treatment of CACS

NGM120 is a proprietary, inhibitory antibody binding GFRAL that is designed to block the effects of elevated GDF15 levels, initially in cancer patients. GDF15 is believed to contribute to uncontrolled weight loss in these patients, also known as CACS, and possibly to the cancer. NGM120 has completed a Phase 1 SAD and MAD clinical trial to assess safety, tolerability and pharmacokinetics in healthy adult subjects and was found to be well tolerated. In the first quarter of 2020, we initiated a multicenter, Phase 1a/1b study that includes two parallel cohorts to evaluate the safety, tolerability and pharmacokinetics, and to obtain preliminary evidence of anti-tumor and anti-CACS activity, of NGM120 in patients with select advanced solid tumors.

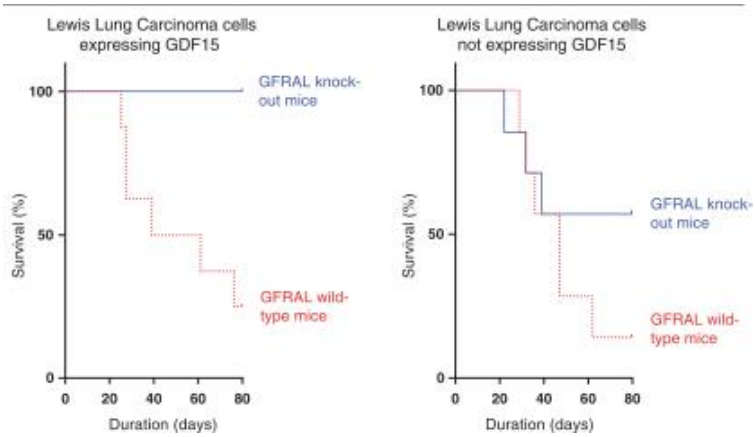
CACS—Cancer Anorexia/Cachexia Syndrome

CACS is a common co-morbidity of cancer and is associated with increased hospitalization and shortened survival compared to cancer patients that do not exhibit cachexia. While cachexia can occur in all types of cancer, particularly high incidence rates are observed in pancreatic, non-small cell lung and gastric cancers, at 54%, 36% and 67% of patients, respectively. Studies have shown that cancer patients that do not experience body weight loss have an improved prognosis. Current therapies targeting CACS are directed towards increasing appetite only; however, there is a lack of approved treatments that also address other aspects of the disease, including muscle mass loss and altered energy metabolism. A direct relationship has been established between GDF15 serum levels and cancer-associated weight loss in humans with certain cancers.

Antagonists to the GDF15/GFRAL Pathway

We believe that inhibitory antibodies blocking the interaction between GFRAL and GDF15 could provide a novel approach to developing treatments for anorexia, CACS and, potentially, cancer. Mice grafted with human tumors overexpressing GDF15 became cachectic, and this weight loss was found to be reversible by treatment with monoclonal antibodies to GDF15. In addition, in a study where Lewis Lung Carcinoma cells engineered to express human GDF15 were injected into wild-type and GFRAL knockout mice, tumor-derived GDF15 appears to impact survival in mice in which the GFRAL signaling pathway is intact, whereas mice lacking GFRAL are resistant to the effects of elevated GDF15 levels. This indicates the potential for anti-GFRAL antibodies to improve patient survival in certain tumor types that express high levels of GDF15, in addition to preserving body mass and preventing development of CACS.

Impact of GDF15 on Survival in Mice Implanted with Lewis Lung Carcinoma Cells

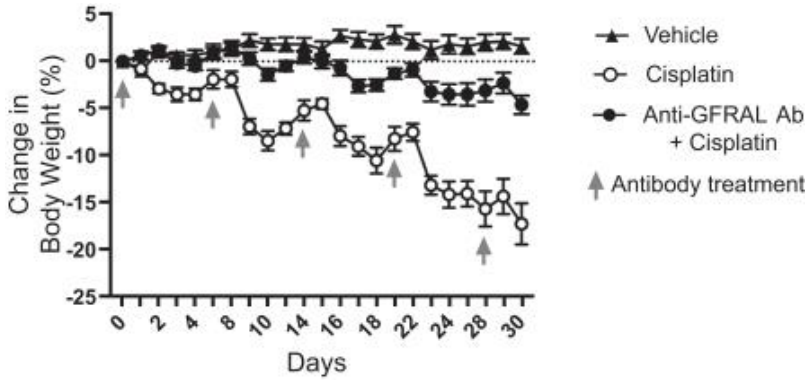


We believe that antibodies against GFRAL will be superior to antibodies against GDF15 because expression levels of GDF15 can rise dramatically in response to infection and other conditions involving cellular insult, meaning that high blood levels of antibodies antagonizing GDF15 will be required to achieve a therapeutic effect. By contrast, GFRAL is expressed at low levels in very specific regions of the brain stem, meaning that a relatively lower blood level of antibodies antagonizing GFRAL will be required to achieve a therapeutic effect.

We believe we have comprehensively characterized the receptor pathway and the structure-function relationship of GDF15 together with its cognate receptor, GFRAL. This understanding facilitated large-scale hybridoma campaigns that generated antibodies targeting key epitopes of the receptor complexes. We have generated and characterized multiple antagonistic antibodies against GFRAL and, from this portfolio, we chose to advance NGM120 as our development candidate.

NGM120, Antagonistic Antibody Against GFRAL

We designed NGM120 as a potent, humanized monoclonal antibody inhibitor of GFRAL with the potential for once-monthly or less frequent dosing. In numerous preclinical pharmacology models, NGM120 reverses and inhibits GDF15-mediated body weight loss and increases in energy expenditure. For example, treatment of mice with cisplatin, a chemotherapy commonly used to treat various cancers, resulted in body weight loss of approximately 15% after 30 days. However, treatment with an anti-GFRAL antibody prevented substantial body weight loss in this model, as shown below:



Preclinical Studies and ongoing Clinical Trials

In extensive preclinical testing, including three-month safety and toxicology studies in non-human primates and rats, NGM120 was well tolerated. NGM120 completed a Phase 1 clinical trial to assess safety, tolerability and pharmacokinetics in healthy adult subjects in 2019. This study demonstrated NGM120 was well tolerated without any identified safety signals and had an expected pharmacokinetic profile.

In the first quarter of 2020, we initiated a multicenter, Phase 1a/1b study to evaluate the safety, tolerability and pharmacokinetics of NGM120 as a monotherapy in patients with select advanced solid tumors (cohort 1) and of NGM120 in combination with gemcitabine and Abraxane® in patients with metastatic pancreatic cancer (cohort 2). Each cohort will consist of an open-label dose-escalation portion followed by a dose-expansion portion. Approximately 90 patients with elevated serum levels of GDF15 are expected to be enrolled in the concurrently run cohorts. Preliminary evidence of anti-tumor and anti-cachexia activity will be assessed by measuring tumor response rates, body mass and composition, patient reported outcomes and functional status. Antagonistic antibodies targeting the GDF15 receptor pathway were not included in the original Merck license to GDF15 analogs, including NGM395 and NGM386, and are subject to Merck's future option upon completion of a human proof-of-concept study.

NGM217: A Potential Treatment for Diabetes

NGM217 is a humanized inhibitory monoclonal antibody against an undisclosed target that has the potential to increase the production of insulin in the pancreas of diabetics by improving effective beta cell function. This improvement is likely to lead to a substantial reduction in glycemic variability, which manifests as hyperglycemia or hypoglycemia in diabetics. We have initiated a Phase 1 clinical trial evaluating the safety and tolerability of NGM217 in patients with diabetes.

Impaired beta cell function leads to the progressive failure of islet cells to secrete sufficient amounts of insulin to overcome peripheral insulin resistance, resulting in failure to maintain normal glucose homeostasis over time. The ability to increase effective beta cell function could be beneficial in three diabetes patient populations: patients with type 1 diabetes; patients with latent autoimmune diabetes in adults (“LADA”); and patients with type 2 diabetes that are inadequately controlled with insulin treatment. In the United States, there are approximately 1.5 million adults with type 1 diabetes, and their functional beta cell mass is unable to produce adequate insulin. LADA is characterized by the slow, progressive autoimmune destruction of beta cells and approximately 10% of patients ages 40 to 75 in the United States with type 2 diabetes have LADA. These patients often become unresponsive to oral type 2 diabetes and GLP-1 therapies, and usually require early use of insulin in order to preserve the remaining pancreatic beta cell function. For these patients, the ability to increase beta cell function closer to onset of disease would provide an additional treatment option beyond insulin. Given the significant unmet medical need among these diabetes patient populations, we believe that NGM217 has the potential to provide a desirable treatment alternative that increases the effective function of beta islet cells while slowing the rate of disease progression.

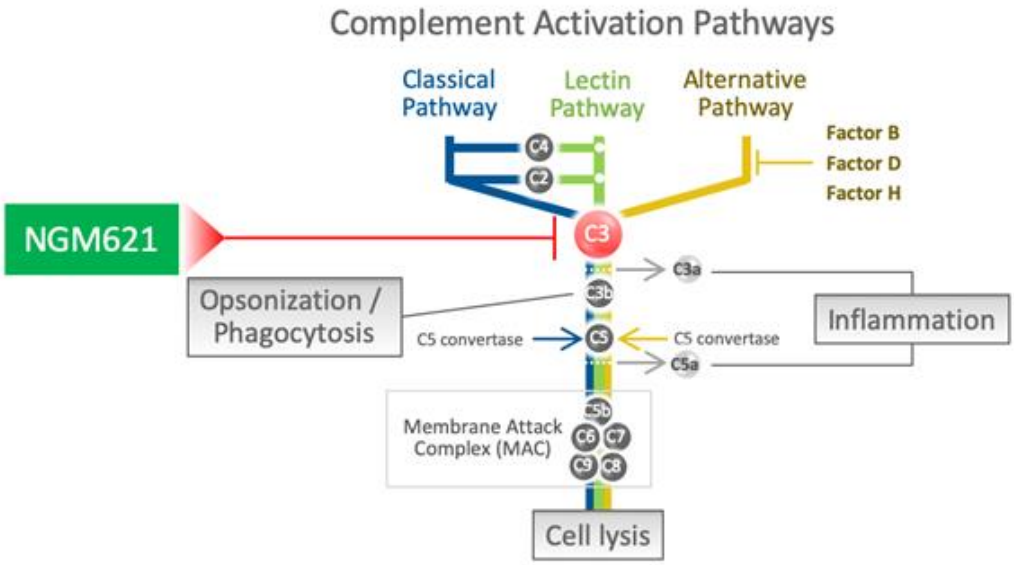
Preclinical Studies and Ongoing Phase 1 Clinical Trial

Preclinical studies assessing the safety of NGM217 demonstrated desirable pharmacokinetics. NGM217 was well tolerated at doses that substantially exceeded the doses to be tested in humans. We have commenced a Phase 1 clinical trial to obtain safety and tolerability data, including rate of hypoglycemia, as well as to select the proper dose for future clinical studies. Based on those results, we plan to commence a Phase 1b/2a proof-of-concept clinical trial in the second half of 2020 to investigate the ability of NGM217 to increase stimulated C-peptide, a marker of insulin production, as well as to reduce insulin requirements and improve glycemic control with no worsening of hypoglycemia.

NGM621: A Potential Treatment for Dry AMD

NGM621 is a humanized inhibitory monoclonal antibody that binds with high affinity to complement C3 and potently blocks complement activation. Human genetics data strongly suggest that dysregulated activation of the complement pathway contributes to AMD and, consequently, that inhibition of complement activation could effectively slow the progression of photoreceptor loss. AMD is the leading cause of vision loss and blindness in people 65 years of age and over in the United States; it is estimated that approximately 3 million people will be affected by AMD in the United States in 2020. AMD is a progressive disease that involves the damage of retina tissue that leads to the development of wet and/or dry AMD, also known as GA. Although treatments for wet AMD are available, no approved treatment is available for dry AMD, which remains a high unmet medical need.

Pathological activation of the complement system has been linked to development and progression of GA by multiple human genetics and animal model studies. A central component of the mammalian immune system, complement can be activated by three main pathways, classical, lectin and alternative, that converge on C3, a master regulator of the complement cascade. Inhibiting complement activation at the level of C3 affords the opportunity to block an array of potentially detrimental downstream effects, including inflammation, cell lysis and opsonization/phagocytosis of photoreceptor cells.



NGM621 binds with high affinity to intact human C3 (K_D=0.34 nM), but shows significantly lower affinity (>100-fold) to C3 cleavage fragments C3a, C3b, C3c, and C3d. This unique binding profile, characterized by high affinity and specificity for intact C3, translated into potent NGM621-mediated inhibition of complement activation via both the alternative (IC_{50} =37 nM) and classical (IC_{50}=74 nM) pathways in *in vitro* hemolytic assays. Furthermore, NGM621 demonstrated *in vivo* activity in an ocular complement activation model in cynomolgus monkeys.

Multiple modalities and classes of complement inhibition therapies are under clinical evaluation in GA patients, although to date, no investigative treatment for GA has shown efficacy in Phase 3. For example, Roche announced in 2017 that lampalizumab, an inhibitor of the alternative complement activation pathway, failed to meet the primary endpoint in two Phase 3 trials in GA. APL-2 (Apellis Pharmaceuticals), a PEGylated peptide inhibitor of C3, only recently entered Phase 3 clinical trials and Zimura® (IVERIC bio), a PEGylated aptamer inhibitor of complement C5, recently completed Phase 2b clinical studies. While APL-2 and Zimura® demonstrated significant reduction in the growth rate of GA lesions in their respective Phase 2 studies, both agents also demonstrated significant increases in the incidence of new onset wet AMD in the eyes being studied. The findings in these clinical trials potentially implicate contributions from complement inhibition and/or polyethylene glycol (“PEG”) modification to the undesirable development of wet AMD in GA patients. However, clinical evidence from several GA trials with complement inhibitors, including lampalizumab, together with large number of studies in nonclinical AMD models, argue against a causative role for complement inhibition in promoting development of wet AMD. In fact, C3 inhibition in a nonclinical model of wet AMD results in a significant reduction of exudation, whereas, in the same model, intravitreal injection of PEG leads directly to an exacerbation of wet AMD. These results are consistent with a potential role of the PEG moiety in the vascular exudation observed in the APL-2 and Zimura® clinical trials.

The evaluation of NGM621, an antibody-based therapeutic, in GA patients will provide an opportunity to test the effects of complement inhibition on disease progression using an agent that lacks PEG modification. Given the significant unmet medical need and the importance of dosing convenience for GA patients, NGM621 has the potential to provide a desirable treatment option with an improved efficacy and safety profile, acting to slow the rate of disease progression with less frequent dosing.

Preclinical Studies and Clinical Trials

IND-enabling preclinical studies for NGM621 were completed in the first half of 2019 and we initiated a Phase 1 SAD and multiple dose clinical trial in the third quarter of 2019 to evaluate the safety, tolerability and pharmacokinetic profile of single and multiple intravitreal injection(s) of NGM621 in GA patients. We also plan to initiate a Phase 2 proof-of-concept clinical trial in the second half of 2020.

Our Collaboration with Merck

Overview and Benefits

In 2015, we entered into a broad, strategic collaboration with Merck in order to advance novel biologic therapeutics for the treatment of highly prevalent diseases with significant unmet medical needs. The collaboration is complementary to our drug development model, and is designed to follow certain approaches used in historically successful collaboration agreements between large pharmaceutical companies and emerging biotechnology companies. The collaboration has provided us with the financial support to broaden and accelerate our existing research efforts, access to mid- and late-stage development expertise and, in the future, would provide us the resources to enable large global trials and the global commercial and distribution capabilities that we believe our products will require. Importantly, this collaboration structure preserves our research independence and allows us to retain meaningful economic rights in our product candidates. In addition, we excluded the aldafermin program from the agreement and it remains wholly owned and controlled by us.

The collaboration included an exclusive worldwide license to our GDF15 receptor agonist program. Effective May 31, 2019, Merck terminated its license to the GDF15 receptor agonist program, returning the NGM395 and NGM386 product candidates to us. Under the agreement, we also granted Merck options to take exclusive, worldwide licenses, on a program-by-program basis, for the programs in our research and development pipeline. Merck generally has a one-time right to exercise its option at the point at which a program completes a human proof-of-concept trial. In November 2018, Merck exercised its option to license our NGM313 program. In March 2019, Merck exercised its option to extend our research collaboration, and thereby preserve its option to license programs in our research and development pipeline, through March 17, 2022. Merck has the right to extend the research collaboration again through March 17, 2024, and is required to inform us of its intent to extend by March 17, 2021.

The strategic value of our agreement with Merck can be summarized as follows:

- ***Financial Support:*** Under the terms of the agreement, Merck paid us an upfront cash licensing fee of $94.0 million and purchased $106.0 million of our Series E convertible preferred stock in 2015. In addition to the upfront cash component, Merck initially committed to provide us research and development reimbursement of up to $50.0 million per year for at least five years. If our research and development expenses exceed $50.0 million in a given year and we are conducting IND-enabling or later-staged activities, Merck is required to elect either to reimburse up to an additional $25.0 million for use in funding IND-enabling or later-staged activities or to provide us with the equivalent value in in-kind services for preclinical and clinical development activities. Therefore, the total Merck reimbursement for our research and development activities could reach $75.0 million per year through the first five years of the research phase, although it only did so for the fiscal year ended December 31, 2019 due to increase in research and development expenses for our ongoing programs. In connection with Merck's exercise of its option to extend our research collaboration in March 2019, Merck agreed to continue to fund our research and development efforts at the same levels during the two-year extension period and, in lieu of a $20.0 million extension fee payable to us, during such two-year extension period Merck will make additional payments totaling up to $20.0 million in support of our research and development activities across 2021 and the first quarter of 2022. Merck also paid us a fee of $20.0 million in December 2018 in connection with the exercise of its license option for NGM313. From inception of the collaboration through December 31, 2019, Merck has paid us $300.5 million of research and development reimbursement.

- ***Economic Opportunity:*** For programs that Merck licenses, we retain an option to participate in the development and commercialization of the drug up to a 50% cost and profit share, which includes an option to co-detail the product alongside Merck in the United States. If we elect to participate in the cost and profit share, subject to certain limitations and in addition to the committed annual funding, Merck has agreed to advance us a portion of our share of the overall development costs, which it will recoup from our share of any profit ultimately resulting from sales of the approved drug or, if unsuccessful, other compounds that reach commercialization and are subject to a cost and profit share. If we decide not to participate in the cost and profit share, Merck will owe us milestone payments and royalties as a percentage of global net sales in the low double digits to mid-teens upon commercialization. Our option to participate in the late-stage development and commercialization of licensed programs, such as NGM313, has not yet been triggered.

- ***A Sharing of Expertise:*** The collaboration provides Merck access to the deep expertise of our team *via* options on the programs emerging from our novel drug discovery approach, while it provides us with a partner experienced in running large, global, late-stage trials focused on population safety and cardiovascular outcome studies. Further, the agreement provides us with access to Merck's substantial commercial capabilities.

- ***Independence and Control Provisions:*** We maintain control over the direction and execution of our research and development program through human proof-of-concept testing, allowing our research team the freedom to seek the most promising candidates and flexibility to terminate or de-prioritize projects. In addition, we excluded aldafermin from the Merck collaboration to retain an independent clinical program and as a means to potentially enable full integration of our capabilities to position us for long-term success.

We believe our pipeline of therapies for the treatment of major diseases, like type 2 diabetes, obesity and NASH, is unusual among emerging biopharmaceutical companies, the uniqueness of which is further evidenced by the broad support provided by our collaboration with Merck. This collaboration provides us with a competitive advantage by enabling us to advance a portfolio of drug candidates in the cardio-metabolic, liver, ophthalmic and oncology areas while still retaining significant economic ownership of the programs.

Summary of the Merck Collaboration Agreement

In 2015, we entered into the Collaboration Agreement with Merck, covering the discovery, development and commercialization of novel therapies across a range of therapeutic areas. In March 2019, Merck exercised its option to extend the collaboration for two additional years, from March 2020 to March 2022. The collaboration included an exclusive worldwide license to our GDF15 program, comprising NGM395 and NGM386 and other GDF15 analogs. Effective March 31, 2019, Merck terminated its license to the program and we regained full rights to the GDF15 receptor agonist program, which includes NGM395 which we are evaluating for the treatment of obesity. The collaboration also includes a broad, multi-year drug discovery and early development program financially supported by Merck but scientifically directed by us with input from Merck. For those compounds resulting from this research and development program that progress through proof-of-concept studies, Merck has an exclusive option, at a cost of $20.0 million for each compound, to obtain an exclusive, worldwide license. If Merck exercises its option with respect to such a compound, we in turn have the right, at the start of the first Phase 3 clinical trial for that compound, to elect to participate in a worldwide cost and profit sharing arrangement with Merck, as well as the option to co-detail the compound in the United States, or we can elect instead to receive milestones and royalties from Merck based on its further development and commercialization of the compound. If we elect to participate in the cost and profit sharing arrangement, subject to certain limitations, Merck will provide us financial assistance in the form of advances of our share of the overall development costs, which it will recoup from our share of any profit ultimately resulting from sales of the compound or, if unsuccessful, other compounds that reach such stage. If the Company does not opt in to the cost and profit sharing option, then the Company is eligible to receive milestone payments upon the achievement of specific clinical development or regulatory events with respect to the licensed compound indications in the United States, EU and Japan of up to an aggregate of $449.0 million.

Research and Early Development Program

Under the agreement, we are conducting an extensive research and early development program, the goal of which is the identification, research and development, through human proof-of-concept studies, of multiple product candidates for various therapeutic areas. Included in this program are all NGM research and development programs that existed when we entered into the agreement with Merck, with the exception of the following: aldafermin, any other compounds that target FGFR4 and inhibit CYP7A1 expression (including variants or derivatives of FGF19) and any compounds that are covered by or within the scope of third party license or option rights. We determine the scientific direction and areas of therapeutic interest, with input from Merck, and we are primarily responsible for the conduct of all research, preclinical and early clinical development activities, through human proof of concept. We make the final determinations as to which compounds to advance into and through initial clinical studies, which to progress into proof-of-concept studies, and the design of any proof-of-concept studies, with input from Merck through various governance committees.

The research and early development program has an initial term of five years, until March 17, 2020. In March 2019, Merck exercised its option to extend the collaboration through March 17, 2022, and has the option to extend it again until March 17, 2024. We refer to this five, seven or, if applicable, nine-year period as the research phase of the collaboration.

Under the agreement, Merck reimbursed the internal and external costs of our research and early development activities in an amount up to $50.0 million per year during the initial five-year term, based on an estimated annual budget. If we exceeded this budget in a particular year, and if we were performing IND-enabling studies at that time, Merck was required to elect either to reimburse up to an additional $25.0 million for use in funding IND-enabling or later-staged activities or to provide us with the equivalent value in in-kind services for preclinical and clinical development activities. Therefore, the total Merck reimbursement for our research and development activities could have reached $75 million per year through the first five years of the research phase, although it only did so for the fiscal year ended December 31, 2019 due to increase in research and development expenses for our ongoing programs. In connection with Merck's exercise of its option to extend our research collaboration in March 2019, Merck agreed to continue to fund our research and development efforts at the same levels during the two-year extension period and, in lieu of a $20.0 million extension fee payable to us, during such two-year extension period Merck will make additional payments totaling up to $20.0 million in support of our research and development activities across 2021 and the first quarter of 2022. From inception of the collaboration through December 31, 2019, Merck has paid us $300.5 million of research and development reimbursement. If Merck elects to extend the research phase for an additional two years, the level of funding that Merck will provide to us during such extension will be negotiated at the time of the extension, subject to certain minimum and maximum funding limits based on a percentage of the then-existing funding. With two exceptions, Merck may not terminate its annual funding of the research and early development program prior to the end of the research phase of the collaboration. Those two exceptions are: (i) if we are acquired by a third party; or (ii) if we are in material uncured breach of our obligations under the research and early development program.

At the end of the research phase, Merck has the right to either require us to continue to conduct research and development activities with respect to certain of the then-existing programs for up to three years, which we call the tail period, by agreeing to pay all our internal and external costs for related work, or to take over such selected programs and conduct such research and development activities itself, at its own cost.

Merck Option to License NGM Programs

During the research phase, or during the tail period, if there is one, following completion of a proof-of-concept study for a particular compound, regardless of the results of such study, Merck has the one-time option to obtain an exclusive, worldwide license, on specified terms, to that compound, as well as to all other molecules that are directed against the same target and that result in the same effect on such target ("Optioned Program"). If Merck exercises its license option, Merck will be responsible, at its own cost, for the further development and any commercialization activities for compounds within that Optioned Program, subject to our options to cost and profit share worldwide, and to co-detail those compounds in the United States, as further described below.

If Merck does not exercise its license option with respect to a particular compound within a limited period of time, we will retain all rights to research, develop and commercialize that compound and its related molecules on a worldwide basis, either alone or in partnership with a third party, subject to the payment to Merck of certain royalties on any commercial sales of any resulting products. If, however, Merck does not exercise its license option because it determined further development of the compound was not warranted for technical, safety or efficacy reasons, and if later in the research phase we again complete a proof-of-concept study with the compound or a related compound, Merck's option rights would nonetheless apply to the compound for a limited period of time. Unless Merck has elected to conduct research and development activities itself, we also retain all rights to programs that have not completed proof-of-concept studies by the end of the research phase, or the tail period, if there is one.

NGM Option to Elect Cost and Profit Share and Merck Financial Assistance

If Merck exercises its license option, then, at the point at which it has advanced the licensed compound to its first Phase 3 clinical trial, we have the option for a limited period of time to participate in a cost and profit sharing arrangement with Merck on that compound. Where we exercise such an option, we call such compounds NGM Optioned Products. As part of our election to exercise our option to cost and profit share, we also select the percentage share—up to 50%—that we desire to fund of the total global costs of developing and, if approved, commercializing that NGM Optioned Product. The percentage of any profits we will receive from sales of the NGM Optioned Product will be the same as the percentage share we elect to contribute to funding costs. Our right to participate in cost and profit sharing under the agreement is subject to the following limitation: if at the point in time when we are exercising our option for a licensed compound the actual costs we have incurred across all NGM Optioned Products, plus the prospective costs allocated to us across all NGM Optioned Products, plus the costs we are electing to incur if we were to exercise our option for the compound, reaches $1.4 billion (if the research phase ends in 2022) or $1.8 billion (if the research phase is extended to 2024), then the Company will not be able to exercise its option on any further licensed compounds that Merck takes forward.

Our agreement also provides that, following our election to cost and profit share on an NGM Optioned Product, Merck will advance to us and/or assume a specified portion of the expected global costs for that NGM Optioned Product. These advances/assumed costs are subject to an aggregate cap across all NGM Optioned Products over the course of the collaboration. We refer to the amount Merck advances/assumes as the Advanced Amount. All Advanced Amounts are treated as an accumulated but deferred cost that we owe to Merck, accrue interest and are recouped by Merck in full out of our share of any profits resulting from sales of that NGM Optioned Product before we receive any of those profits. If an NGM Optioned Product fails to generate profit sufficient to repay the balance of the Advanced Amount, the balance will be carried forward and recouped out of profits resulting from sales of any subsequent NGM Optioned Product(s), even if we did not obtain any advances from Merck on our share of costs for such subsequent NGM Optioned Product. We are responsible for directly funding all global development and commercialization costs of an NGM Optioned Product that are over and above any Advanced Amount.

Co-Detailing Rights in the United States

For each NGM Optioned Product, we also have the option to participate in a portion of the commercial promotion, which we refer to as co-detailing, to provide up to 25% of the total requisite details in the United States of that NGM Optioned Product by fielding our own commercial sales force. We are required to make this election prior to receiving regulatory approval in the United States for the NGM Optioned Product. The specifics of our participation in co-detailing will be determined by the parties according to guidelines set out in the agreement. If we elect to co-detail with Merck, our costs are included in the overall shared commercialization costs, but we do not share in any greater portion of the profits than we otherwise would be entitled to for that NGM Optioned Product.

Small Molecule Research and Development

Under our agreement we also granted Merck a worldwide, exclusive right to conduct research and development on, and to manufacture, use and commercialize, small molecule compounds identified or developed by Merck that have specified activity against any target that we are researching or developing under the research and early development program and that, but for use of our confidential and proprietary information, Merck would not have discovered. If Merck ultimately does not exercise its license option to the compound we have taken through a proof-of-concept study that is directed to any such target, Merck's research license for its own small molecule program with respect to such target will become non-exclusive, but it will retain an exclusive license to any small molecule compounds that it has as of that time identified and developed. Merck has sole responsibility for research and development of any of these small molecule compounds, at its own cost. We are eligible to receive milestone and royalty payments on small molecule compounds that are developed by Merck under our license, in some cases at the same rates as those we are eligible to receive from Merck for a licensed program originating from our own research and development efforts, provided that, but for use of our confidential and proprietary information, Merck would not have discovered such small molecule compounds. However, we do not have the option to cost and profit share or the option to co-detail those small molecule products.

Collaboration Governance

Our collaboration with Merck is managed by a set of joint committees composed of equal numbers of representatives from each of us and Merck. A joint research committee has been established to review and discuss the preclinical work that we are conducting and to solicit Merck's input on our research activities. Once we nominate a clinical candidate, a joint early development committee oversees and facilitates the conduct of preclinical and early development activities. For NGM313 and any other Optioned Program, a joint late development committee oversees and coordinates development. A joint commercialization committee will oversee the commercialization of any compound arising from an Optioned Program as to which we elect to cost and profit share. Decision making in these committees generally requires the agreement of both Merck's and our representatives, with unresolved issues escalating through to certain executive officers, and with us having the final say with respect to research and early development program matters and Merck having final say with respect to Optioned Program matters and late development and commercialization matters following the exercise of its option for a particular program.

Diligence

We and Merck must each use commercially reasonable efforts to perform all of our respective activities under the collaboration.

Exclusivity

During the research phase, we may not directly or indirectly research, develop, manufacture or commercialize, outside of the collaboration, any product with specified activity against any target that we are researching or developing under the collaboration. After the research phase, if Merck exercises its license option for a program, we may not directly or indirectly research, develop, manufacture or commercialize any product with specified activity against the target that is the subject of that licensed program for so long as Merck's license to that program remains in effect.

Financial Terms

In exchange for these various rights and access to our drug discovery approach, Merck paid us an upfront cash fee of $94.0 million and purchased approximately $106.0 million of our Series E convertible preferred stock. In connection with Merck's exercise of its option to extend our research collaboration in March 2019, Merck agreed to continue to fund our research and development efforts at the same levels during the two-year extension period and, in lieu of a $20.0 million extension fee payable to us, during such two-year extension period Merck will make additional payments totaling up to $20.0 million in support of our research and development activities across 2021 and the first quarter of 2022. We are entitled to receive an extension payment of $20.0 million from Merck if it chooses to further extend the extended research phase until March 17, 2024.

If Merck exercises its license option following completion of a human proof-of-concept study, Merck is required to pay us an option fee of $20.0 million for each licensed program. In December 2018, we received a $20.0 million payment from Merck in connection with the exercise of its license option for the NGM313 program.

If we do not elect to enter into a cost and profit sharing arrangement for a compound we have licensed to Merck including NGM313, we are eligible to receive an aggregate of $449.0 million in milestone payments, of which $77.7 million relates to the potential achievement of specific clinical development events and $371.3 million relates to the potential achievement of certain regulatory events with respect to the licensed compounds for the first three indications in the United States, EU and Japan.

A breakout of the milestone payments in connection with the potential achievement of certain clinical development events is as follows (in thousands):

	First Indication	Second Indication	Third Indication
Upon administration of an applicable product to the first patient in the first Phase 3 clinical trial for such product for the given indication	$ 35,000	$ 25,250	$ 17,500

A breakout of the milestone payments in connection with the potential achievement of various regulatory events for each of the three indications, for each of the three geographic areas, is as follows (in thousands):

	First Indication	Second Indication	Third Indication	Total
United States	$ 75,000	$ 56,250	$ 37,500	$ 168,750
European Union	60,000	45,000	30,000	135,000
Japan	30,000	22,500	15,000	67,500
	$ 165,000	$ 123,750	$ 82,500	$ 371,250

We are also eligible to receive commercial milestone payments of up to $125.0 million payable for such licensed product. We are also eligible to receive royalties at ascending low double digit to mid-teen percentage rates, depending on the level of net sales Merck achieves worldwide for each licensed compound.

If Merck does not exercise its license option to a compound and we commercialize that compound or its related molecules, we will owe Merck royalties at low single digit rates. If Merck exercises its license option but then terminates its license to a program, such as the GDF15 receptor agonist program, and we take compounds in that program forward, we also owe Merck royalties on sales of those compounds, at low single digit rates.

Termination

After the research phase, Merck may terminate the overall agreement for convenience upon written notice. Subject to certain limitations, Merck may partially terminate the agreement for convenience as it relates to any Optioned Program, such as NGM313, on written notice. It may also terminate the agreement as it relates to its rights to research and develop small molecule compounds.

Either we or Merck may terminate the agreement with respect to a specific Optioned Program if the other party is in material breach of its obligations regarding that specific program and fails to cure the breach within the specified cure period. If Merck terminates a program as a result of our uncured material breach, then we would lose our option to participate in global cost and profit sharing if not yet exercised as of the time of termination, and lose our co-detailing option (whether or not exercised as of that time) for compounds arising from the relevant Optioned Program and if Merck terminates for our breach with respect to an Optioned Program and there are no other Optioned Programs at such time, then we would also be required to commence repaying any Advanced Amounts outstanding with respect to such Optioned Products. If we had exercised our option to participate in global cost and profit sharing of one or more licensed compounds arising from the program as of the time of termination, the option would remain in effect.

If we terminate an Optioned Program for uncured breach by Merck, or if Merck terminates a program for convenience, all licenses granted to Merck with respect to such program will terminate and Merck will grant to us an exclusive license under Merck’s intellectual property related to the terminated program for use in the further development and commercialization of products arising under the terminated program, subject to the payment of a modest royalty back to Merck, assign to us all related regulatory filings and approvals, and provide certain other transition assistance to us.

Merck also has the right to terminate the agreement for convenience, and for uncured material breach by us, on written notice as it relates to its license to any particular licensed small molecule compound. We in turn have the right to terminate if Merck has failed to cure any material breach as it relates to any licensed small molecule compound. If Merck terminates for convenience, or we terminate for such breach by Merck, all licenses to Merck with respect to the relevant small molecule compound terminate, but Merck retains all interest in and to the actual small molecule compound it had developed. If Merck terminates for our uncured material breach, we would continue to receive the full amount of milestones and royalties we were otherwise eligible for with respect to the relevant compounds, but we would lose our rights to participate in the various governance committees as they relate to those small molecule program compounds.

Effect of our Change in Control and Certain Competitive Acquisitions

If we undergo any change in control, which includes the acquisition of us by any third party, or the sale of all or substantially all of our assets relating to the Merck agreement to a third party, or the sale of more than 50% of our voting stock to a third party, Merck has the right to terminate our research and early development program, in its entirety, or only with respect to certain of the programs then being pursued. If it does so, all funding for the terminated programs would cease, and we would transition, at Merck's expense, to Merck any clinical studies then being conducted by us, if directed by Merck. If Merck takes over the studies, it would continue to have the option to license a particular program upon completion of the first proof-of-concept study, but if Merck ceases development of the compounds prior to such proof-of-concept study, the program would revert back to us and Merck would have no further rights.

If our change in control involves another pharmaceutical company with significant annual sales of pharmaceutical products, which we refer to as a Pharma Acquisition, Merck would have certain additional rights which could only be exercised within the first year following the Pharma Acquisition. These include: limiting our right to cost and profit share; Merck ceasing to provide any additional Advanced Amounts with respect to one or more Optioned Programs; and requiring us to repay any or all then-outstanding Advanced Amounts, plus interest, in installments; and termination of our co-detailing rights. Merck would also have the right following any Pharma Acquisition to terminate or restrict our participation on our various governance committees, and to limit the information it provides to us to higher level summaries.

If our acquirer in the event of a change in control is at that time pursuing research, development, commercialization, manufacturing or otherwise has any rights to any compounds that modulate a target that is the subject of an Optioned Program, which we refer to as a Competing Mature Program, Merck also has certain rights, unless our acquirer elects to cease those research, development and commercialization activities. These rights include: Merck ceasing to provide any additional Advanced Amounts with respect to any compounds arising from the Optioned Program that have the same target as the Competing Mature Program, and requiring us to repay any or all then-outstanding Advanced Amounts, plus interest, in installments, with respect to any compounds arising from that Optioned Program, and termination of our co-detailing rights with respect to the relevant compounds, termination of our participation in governance committees with respect to those compounds, and restrictions on the information we receive from Merck with respect to the compounds. However, our rights to share in costs/profits with respect to any such compounds, if exercised, would remain in effect, as would any milestone or royalty payment obligations of Merck with respect to the compounds.

In addition, if our acquirer in the event of a change in control is at that time researching, developing, manufacturing or otherwise has rights to any compounds that modulate a target that is also being actively pursued under our research and early development program, and which has not reached the proof-of-concept study stage but is ready for preclinical development, which we refer to as a Competing Early Program, Merck has the right to require us to select either to provide information demonstrating that the Competing Early Program does not actually modulate the relevant target in the same manner as our candidate, or to contribute the Competing Early Program to our collaboration with Merck as though it had originated under our research and early development program, or to divest the Competing Early Program. If we contribute the Competing Early Program to our collaboration with Merck, all the same financial obligations of Merck would apply, and we would retain all of our option rights with respect to the relevant compounds if Merck exercises its license option when the first compound arising under the program completes the first proof-of-concept study.

Equity Investments by Merck

Concurrently with the execution of our collaboration with Merck, we entered into a stock purchase agreement with Merck for the purchase of 8,833,333 shares of our Series E convertible preferred stock, for an aggregate purchase price of approximately $106.0 million. In addition, concurrent to the closing of our initial public offering ("IPO") in April 2019, we issued 4,121,683 shares of our common stock to Merck in a private placement at a price of $16.00 per share for proceeds of $65.9 million, which resulted in Merck owning approximately 19.9% of our outstanding shares. If Merck elects to further extend the research phase of our collaboration until March 17, 2024, it has the option to purchase an additional $5.0 million of our common stock at a price per share equal to the last closing price of our shares on the date it notifies us of its desire to exercise such option, with such option subject to an overall cap on Merck's ownership interest of 19.9%.

Government Regulation and Product Approval

The FDA and other regulatory authorities at federal, state and local levels, as well as in foreign countries, extensively regulate, among other things, the research, development, testing, manufacture, quality control, import, export, safety, effectiveness, labeling, packaging, storage, distribution, record keeping, approval, advertising, promotion, marketing, post-approval monitoring and post-approval reporting of biologics, such as those we are developing. We, along with third-party contractors, will be required to navigate the various preclinical, clinical and commercial approval requirements of the governing regulatory agencies of the countries in which we wish to conduct studies or seek approval or licensure of our product candidates.

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

- completion of preclinical laboratory tests and animal studies performed in accordance with the FDA's current Good Laboratory Practice regulation;
- submission to the FDA of an IND which must become effective before clinical trials may begin and must be updated annually or when significant changes are made;
- approval by an independent Institutional Review Board ("IRB"), or ethics committee at each clinical site before the trial is commenced;
- performance of adequate and well-controlled human clinical trials to establish the safety, purity and potency of the proposed biologic product candidate for its intended purpose;
- preparation of and submission to the FDA of a BLA after completion of all pivotal clinical trials;
- a determination by the FDA within 60 days of its receipt of a BLA to file the application for review;
- satisfactory completion of an FDA Advisory Committee review, if applicable;
- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the proposed product is produced to assess compliance with current Good Manufacturing Practices ("cGMP"), and to assure that the facilities, methods and controls are adequate to preserve the biological product's continued safety, purity and potency, and of selected clinical investigation sites to assess compliance with current Good Clinical Practices ("cGCP"); and
- FDA review and approval of the BLA to permit commercial marketing of the product for particular indications for use in the United States.

Preclinical and Clinical Development

Prior to beginning the first clinical trial with a product candidate, an IND sponsor must submit an IND to the FDA. An IND is a request for authorization from the FDA to administer an IND product to humans. The central focus of an IND submission is on the general investigational plan and the protocol(s) for clinical studies. The IND also includes results of animal and in vitro studies assessing the toxicology, pharmacokinetics, pharmacology, and pharmacodynamic characteristics of the product; chemistry, manufacturing, and controls information; and any available human data or literature to support the use of the investigational product. An IND must become effective before human clinical trials may begin. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises safety concerns or questions about the proposed clinical trial. 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 the clinical trial can begin. Submission of an IND therefore may or may not result in FDA authorization to begin a clinical trial.

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with cGCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical study. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A separate submission to the existing IND must be made for each successive clinical trial conducted during product development and for any subsequent protocol amendments. Furthermore, an independent IRB for each site proposing to conduct the clinical trial must review and approve the plan for any clinical trial and its informed consent form before the clinical trial begins at that site, and must monitor the study until completed. Regulatory authorities, the IRB or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk or that the trial is unlikely to meet its stated objectives. Some studies also include oversight by an independent group of qualified experts organized by the clinical study sponsor, known as a data safety monitoring board, which provides authorization for whether or not a study may move forward at designated check points based on access to certain data from the study and may halt the clinical trial if it determines that there is an unacceptable safety risk for subjects or other grounds, such as no demonstration of efficacy. There are also requirements governing the reporting of ongoing clinical studies and clinical study results to public registries.

For purposes of BLA approval, human clinical trials are typically conducted in three sequential phases that may overlap.

- ***Phase 1—***The investigational product is initially introduced into healthy human subjects or patients with the target disease or condition. These studies are designed to test the safety, dosage tolerance, absorption, metabolism and distribution of the investigational product in humans, the side effects associated with increasing doses and, if possible, to gain early evidence on effectiveness.

- ***Phase 2—***The investigational product is administered to a limited patient population with a specified disease or condition to evaluate the preliminary efficacy, optimal dosages and dosing schedule and to identify possible adverse side effects and safety risks. Multiple Phase 2 clinical trials may be conducted to obtain information prior to beginning larger and more expensive Phase 3 clinical trials.

- ***Phase 3—***The investigational product is administered to an expanded patient population to further evaluate dosage, to provide statistically significant evidence of clinical efficacy and to further test for safety, generally at multiple geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk/benefit ratio of the investigational product and to provide an adequate basis for product approval.

In some cases, the FDA may require, or companies may voluntarily pursue, additional clinical trials after a product is approved to gain more information about the product. These are called Phase 4 studies and may be made a condition to approval of the BLA. Concurrent with clinical trials, companies may complete additional animal studies and develop additional information about the biological characteristics of the product candidate, and must finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, for biologics, must develop methods for testing the identity, strength, quality, purity and potency of the product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

BLA Submission and Review

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, the results of product development, nonclinical studies and clinical trials are submitted to the FDA as part of a BLA requesting approval to market the product for one or more indications. The BLA must include all relevant data available from pertinent preclinical and clinical studies, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls, and proposed labeling, among other things. The submission of a BLA requires payment of a substantial application user fee to FDA, unless a waiver or exemption applies.

Once a BLA has been submitted, the FDA generally makes a decision on the acceptance of the application for filing within 60 days of receipt. The FDA's goal is to review standard applications within ten months after it accepts the application for filing, or, if the application qualifies for priority review, six months after the FDA accepts the application for filing. In both standard and priority reviews, the review process is often significantly extended by FDA requests for additional information or clarification. The FDA reviews a BLA to determine, among other things, whether a product is safe, pure and potent and the facility in which it is manufactured, processed, packed or held meets standards designed to assure the product's continued safety, purity and potency. The FDA may convene an advisory committee to provide clinical insight on application review questions. Before approving a BLA, the FDA will typically inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure compliance with cGCP. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

After the FDA evaluates a BLA and conducts inspections of manufacturing facilities where the investigational product and/or its drug substance will be produced, the FDA may issue an approval letter or a Complete Response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A Complete Response letter will describe all of the deficiencies that the FDA has identified in the BLA, except that where the FDA determines that the data supporting the application are inadequate to support approval, the FDA may issue the Complete Response letter without first conducting required inspections, testing submitted product lots and/or reviewing proposed labeling. In issuing the Complete Response letter, the FDA may recommend actions that the applicant might take to place the BLA in condition for approval, including requests for additional information or clarification. The FDA may delay or refuse approval of a BLA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and surveillance to monitor safety or efficacy of a product.

If regulatory approval of a product is granted, such approval will be granted for particular indications and may entail limitations on the indicated uses for which such product may be marketed. For example, the FDA may approve the BLA with a Risk Evaluation and Mitigation Strategy ("REMS") to ensure the benefits of the product outweigh its risks. A REMS is a safety strategy to manage a known or potential serious risk associated with a product and to enable patients to have continued access to such medicines by managing their safe use, and could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling or the development of adequate controls and specifications. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing requirements is not maintained or if problems occur after the product reaches the marketplace. The FDA may require one or more Phase 4 post-marketing studies and surveillance to further assess and monitor the product's safety and effectiveness after commercialization, and may limit further marketing of the product based on the results of these post-marketing studies.

Accelerated Approval Program

Any marketing application for a biologic submitted to the FDA for approval may be eligible for FDA programs intended to expedite the FDA review and approval process, such as priority review and accelerated approval. A product is eligible for priority review if it has the potential to provide a significant improvement in the treatment, diagnosis or prevention of a serious disease or condition compared to marketed products. For products containing new molecular entities, priority review designation means the FDA's goal is to take action on the marketing application within six months of the 60-day filing date (compared with ten months under standard review).

Additionally, products studied for their safety and effectiveness in treating serious or life-threatening diseases or conditions may receive accelerated approval (Subpart H and E regulations) upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, 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 accelerated approval, the FDA will generally require the sponsor to perform adequate and well-controlled post-marketing clinical studies to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. In addition, the FDA currently requires, as a condition for accelerated approval, pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

Priority review and accelerated approval do not change the standards for approval but may expedite the development or approval process.

Orphan Drug Designation

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

If a product 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 exclusive approval (or exclusivity), which means that the FDA may not approve any other applications, including a full BLA, to market the same biologic for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity. Orphan drug exclusivity does not prevent FDA from approving a different drug or biologic for the same disease or condition, or the same drug or biologic 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 BLA application fee.

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. In addition, 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 quantities of the product to meet the needs of patients with the rare disease or condition.

Post-Approval Requirements

Any products manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to record-keeping, reporting of adverse experiences, periodic reporting, product sampling and distribution, and advertising and promotion of the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing user fee requirements, under which FDA assesses an annual program fee for each product identified in an approved BLA. Biologic manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP, which impose certain procedural and documentation requirements upon sponsors and their third-party manufacturers. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting requirements upon sponsors and their third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical studies to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of a product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical studies;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of existing product approvals;
- product seizure or detention, or refusal of the FDA to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA closely regulates the marketing, labeling, advertising and promotion of biologics. A company can make only those claims relating to safety and efficacy, purity and potency that are approved by the FDA and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products.

Biosimilars and Reference Product Exclusivity

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, the "ACA"), signed into law in 2010, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009 ("BPCIA"), which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-approved reference biological product.

Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity and potency, can be shown through analytical studies, animal studies and a clinical study or studies. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product in any given patient and, for products that are administered multiple times to an individual, the biologic and the reference biologic may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing that applicant's own preclinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of its product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products.

The BPCIA is complex and continues to be interpreted and implemented by the FDA. In addition, recent government proposals have sought to reduce the 12-year reference product exclusivity period. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. As a result, the ultimate impact and implementation of the BPCIA is subject to significant uncertainty.

Other U.S. Healthcare Laws and Compliance Requirements

In the United States, our current and future operations are subject to regulation by various federal, state and local authorities in addition to the FDA, including but not limited to, the Centers for Medicare and Medicaid Services ("CMS"), other divisions of the United States Department of Health and Human Services ("HHS") (such as the Office of Inspector General, Office for Civil Rights and the Health Resources and Service Administration), the U.S. Department of Justice ("DOJ"), and individual U.S. Attorney offices within the DOJ, and state and local governments. For example, our clinical research, sales, marketing and scientific/educational grant programs may have to comply with the anti-fraud and abuse provisions of the Social Security Act, the false claims laws, the privacy and security provisions of the Health Insurance Portability and Accountability Act ("HIPAA") and similar state laws, each as amended, as applicable.

The federal Anti-Kickback Statute prohibits, among other things, any person or entity, from knowingly and willfully offering, paying, soliciting or receiving any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any item or service reimbursable, in whole or in part, under Medicare, Medicaid or other federal healthcare programs. The term remuneration has been interpreted broadly to include anything of value. The Anti-Kickback Statute has been interpreted to apply to arrangements between therapeutic product manufacturers on one hand and prescribers, purchasers and formulary managers on the other. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution. The exceptions and safe harbors are drawn narrowly and practices that involve remuneration that may be alleged to be intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances. Our practices may not in all cases meet all of the criteria for protection under a statutory exception or regulatory safe harbor.

Additionally, the intent standard under the Anti-Kickback Statute was amended by the ACA to a stricter standard such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the ACA codified case law that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act ("FCA").

The federal false claims and civil monetary penalty laws, including the FCA, which imposes significant penalties and can be enforced by private citizens through civil *qui tam* actions, prohibit any person or entity from, among other things, knowingly presenting, or causing to be presented, a false or fraudulent claim for payment to, or approval by, the federal government, including federal healthcare programs, such as Medicare and Medicaid, knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government, or knowingly making a false statement to improperly avoid, decrease or conceal an obligation to pay money to the federal government. A claim includes "any request or demand" for money or property presented to the U.S. government. For instance, historically, pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of the product for unapproved, off-label, and thus generally non-reimbursable, uses.

HIPAA created additional federal criminal statutes that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud or to obtain, by means of false or fraudulent pretenses, representations or promises, any money or property owned by, or under the control or custody of, any healthcare benefit program, including private third-party payors, willfully obstructing a criminal investigation of a healthcare offense and knowingly and willfully falsifying, concealing or covering up by trick, scheme or device, 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. Like the Anti-Kickback Statute, the ACA amended the intent standard for certain healthcare fraud statutes under HIPAA such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

Also, many states have similar, and typically more prohibitive, fraud and abuse statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

We may be subject to data privacy and security regulations 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 its implementing regulations, imposes requirements 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, independent contractors or agents of covered entities that receive or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also created four 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 HIPAA and seek attorneys' fees and costs associated with pursuing federal civil actions. In addition, many state laws govern the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways, are often not pre-empted by HIPAA, and may have a more prohibitive effect than HIPAA, thus complicating compliance efforts.

We may develop products that, once approved, may be administered by a physician. Under currently applicable U.S. law, certain products not usually self-administered (including injectable drugs) may be eligible for coverage under Medicare through Medicare Part B. Medicare Part B is part of original Medicare, the federal health care program that provides health care benefits to the aged and disabled, and covers outpatient services and supplies, including certain pharmaceutical products, that are medically necessary to treat a beneficiary's health condition. As a condition of receiving Medicare Part B reimbursement for a manufacturer's eligible drugs, the manufacturer is required to participate in other government healthcare programs, including the Medicaid Drug Rebate Program and the 340B Drug Pricing Program. The Medicaid Drug Rebate Program requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of HHS as a condition for states to receive federal matching funds for the manufacturer's outpatient drugs furnished to Medicaid patients. Under the 340B Drug Pricing Program, the manufacturer must extend discounts to entities that participate in the program.

In addition, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average sales price and best price. Penalties may apply in some cases when such metrics are not submitted accurately and timely. Further, these prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. It is difficult to predict how Medicare coverage and reimbursement policies will be applied to our products in the future and coverage and reimbursement under different federal healthcare programs are not always consistent. Medicare reimbursement rates may also reflect budgetary constraints placed on the Medicare program.

Additionally, the federal Physician Payments Sunshine Act (the "Sunshine Act"), within the ACA, and its implementing regulations, require that certain manufacturers of drugs, devices, biological and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) report annually to CMS information related to certain payments or other transfers of value made or distributed to physicians and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals and to report annually certain ownership and investment interests held by physicians and their immediate family members. Failure to report accurately could result in penalties.

In addition, many states also govern the reporting of such payments or other transfers of value, many of which differ from each other in significant ways, are often not pre-empted and may have a more prohibitive effect than the Sunshine Act, thus further complicating compliance efforts.

In order to distribute products commercially, we must comply with state laws that require the registration of manufacturers and wholesale distributors of drug and biological products in a state, including, in certain states, manufacturers and distributors who ship products into the state even if such manufacturers or distributors have no place of business within the state. Some states also impose requirements on manufacturers and distributors to establish the pedigree of product in the chain of distribution, including some states that require manufacturers and others to adopt new technology capable of tracking and tracing product as it moves through the distribution chain. Several states have enacted legislation requiring pharmaceutical and biotechnology companies to establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales, marketing, pricing, clinical trials and other activities and/or register their sales representatives, as well as to prohibit pharmacies and other healthcare entities from providing certain physician prescribing data to pharmaceutical and biotechnology companies for use in sales and marketing, and to prohibit certain other sales and marketing practices. All of our activities are potentially subject to federal and state consumer protection and unfair competition laws.

Ensuring business arrangements with third parties comply with applicable healthcare laws and regulations is a costly endeavor. If our operations are found to be in violation of any of the federal and state healthcare laws described above or any other current or future governmental regulations that apply to us, we may be subject to penalties, including without limitation, civil, criminal and/or administrative penalties, damages, fines, disgorgement, individual imprisonment, exclusion from participation in government programs, such as Medicare and Medicaid, injunctions, private *qui tam* actions brought by individual whistleblowers in the name of the government, or refusal to allow us to enter into government contracts, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, additional reporting obligations and oversight if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we may obtain regulatory approval. In the United States and in foreign markets, sales of any products for which we receive regulatory approval for commercial sale will depend, in part, on the extent to which third-party payors provide coverage and establish adequate reimbursement levels for such products. In the United States, third-party payors include federal and state healthcare programs, private managed care providers, health insurers and other organizations. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid in the United States, and commercial payors are critical to new product acceptance.

Our ability to commercialize any products successfully also will depend, in part, on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which therapeutics they will pay for and establish reimbursement levels. Coverage and reimbursement by a third-party payor may depend upon a number of factors, including the third-party payor’s determination that use of a therapeutic is:

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

We cannot be sure that reimbursement will be available for any product that we commercialize and, if coverage and reimbursement are available, what the level of reimbursement will be. Coverage may also be more limited than the purposes for which the product is approved by the FDA or comparable foreign regulatory authorities. Reimbursement may impact the demand for, or the price of, any product for which we obtain regulatory approval.

Third-party payors are increasingly challenging the price, examining the medical necessity and reviewing the cost-effectiveness of medical products, therapies and services, in addition to questioning their safety and efficacy. Obtaining reimbursement for our products may be particularly difficult because of the higher prices often associated with branded drugs and drugs administered under the supervision of a physician. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain FDA approvals. Our product candidates may not be considered medically necessary or cost-effective. Obtaining coverage and reimbursement approval of a product from a government or other third-party payor is a time-consuming and costly process that could require us to provide to each payor supporting scientific, clinical and cost-effectiveness data for the use of our product on a payor-by-payor basis, with no assurance that coverage and adequate reimbursement will be obtained. A payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage for the product. 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. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize any product candidate that we successfully develop.

Different pricing and reimbursement schemes exist in other countries. In the EU, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost effectiveness of a particular product candidate to currently available therapies. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on health care costs has become intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country.

The marketability of any product candidates 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, emphasis on managed care, the increasing influence of health maintenance organizations and additional legislative changes in the United States have increased, and we expect will continue to increase, the pressure on healthcare pricing. The downward pressure on the rise in healthcare costs in general, particularly prescription medicines, medical devices and surgical procedures and other treatments, has become very intense. 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.

Healthcare Reform

In the United States and some foreign jurisdictions, there have been, and continue to be, several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of product candidates, restrict or regulate post-approval activities, and affect the ability to profitably sell product candidates for which marketing approval is obtained. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives.

For example, the ACA has substantially changed healthcare financing and delivery by both governmental and private insurers. Among the ACA provisions of importance to the pharmaceutical and biotechnology industries are the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain specified branded prescription drugs and biologic agents apportioned among these entities according to their market share in some government healthcare programs;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the Average Manufacturer Price ("AMP") for most branded and generic drugs, respectively, and capped the total rebate amount for innovator drugs at 100% of the AMP;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts, which through subsequent legislative amendments, were increased to 70% in 2019, off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability;
- expansion of the entities eligible for discounts under the 340B Drug Discount Program;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- expansion of healthcare fraud and abuse laws, including the FCA and the Anti-Kickback Statute, new government investigative powers, and enhanced penalties for noncompliance;
- 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;
- requirements to report certain financial arrangements with physicians and teaching hospitals; and
- establishment of a Center for Medicare and Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending.

There have been legal and political challenges to certain aspects of the ACA. Since January 2017, President Trump has signed two executive orders and other directives designed to delay, circumvent or loosen certain requirements mandated by the ACA. The ultimate content, timing or effect of any healthcare reform legislation on the U.S. healthcare industry is unclear.

We anticipate that the ACA, if substantially maintained in its current form, will continue to result in additional downward pressure on coverage and the price that we receive for any approved product, and could seriously harm our business. Any reduction in reimbursement from Medicare and other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products. Such reforms could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop product candidates.

Further legislation or regulation could be passed that could harm our business, financial condition and results of operations. Other legislative changes have been proposed and adopted since the ACA was enacted. Aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect beginning on April 1, 2013, will stay in effect through 2027 unless additional Congressional action is taken.

Additionally, there has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed federal 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. The Trump administration released a “Blueprint”, or plan, to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase drug 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 HHS 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. While some proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. Individual states in the United States have also become increasingly active in passing legislation and implementing 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.

The Foreign Corrupt Practices Act

The Foreign Corrupt Practices Act (“FCPA”), prohibits any U.S. individual or business from paying, offering or authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with accounting provisions requiring us to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Environmental Regulation

In addition to the foregoing, state and federal laws regarding safe working conditions, environmental protection and hazardous substances, including the Occupational Safety and Health Act, the Resource Conservancy and Recovery Act and the Toxic Substances Control Act, affect our business. These and other laws govern our use, handling and disposal of various biological, chemical and radioactive substances used in, and wastes generated by, our operations. We may incur significant costs to comply with such laws and regulations now or in the future. If our operations result in contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and governmental fines. We believe that we are in material compliance with applicable environmental laws and that continued compliance therewith will not have a material adverse effect on our business. We cannot predict, however, how changes in these laws may affect our future operations.

Competition

The biopharmaceutical industry is characterized by intense competition and rapid innovation. Although we believe that we hold a strong position in research in certain areas of cardio-metabolic disease, NASH, ophthalmology and cancer, our competitors may be able to develop other compounds or drugs that are able to achieve similar or better results. Our competitors include multinational pharmaceutical companies, specialized biotechnology companies and universities and other research institutions. Smaller or earlier-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. We believe the key competitive factors that will affect the development and commercial success of our product candidates are their efficacy, safety and tolerability profile, reliability, convenience of dosing, pricing, the level of generic competition and reimbursement.

There are many pharmaceutical companies, biotechnology companies, public and private universities and research organizations actively engaged in the research and development of products that may be competitive to our products. A number of pharmaceutical companies, including AbbVie, Allergan, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Eisai, Eli Lilly, GlaxoSmithKline, Johnson & Johnson, Merck, Novartis, Novo Nordisk, Pfizer, Roche, Sanofi and Takeda, as well as large and small biotechnology companies such as 89Bio, Akero, Albireo, Alentis, Amgen, Apellis, Ascletis, Axcella, Bird Rock, Can-Fite, Cirius, Enanta, Galectin, Galmed, Genfit, Gilead, Glympse, Immuron, Intercept, Inventiva, Iveric, Madrigal, MannKind, MediciNova, Metacrine, Mirum, Nalpropion, North Sea, Promethera, Salix, Scholar Rock, Seal Rock, Terns, Tiziana, Viking and Vivus, are pursuing the development or marketing of pharmaceuticals that target the same diseases that we are targeting. It is probable that the number of companies seeking to develop products and therapies for the treatment of metabolic disorders, liver, oncologic and ophthalmic diseases will increase. For example, we are aware of other companies, including Enanta, Gilead, Intercept, Metacrine, Novartis and Terns that are seeking to develop FXR agonist drug candidates that modulate FGF19. Many of these and other existing or potential competitors have substantially greater financial, technical, human and other resources than we have and may be better equipped to develop, manufacture and market products. These companies may develop and introduce products and processes competitive with or superior to ours. In addition, other technologies or products may be developed that have an entirely different approach or means of accomplishing the intended purposes of our products, which might render our technology and products noncompetitive or obsolete.

There are currently no FDA-approved products for the treatment of NASH. If aldafermin or NGM313 are approved for the treatment of NASH, competition could arise from products currently in development, including: cenicriviroc, an immunomodulator that blocks CCR2 and CCR5 from Allergan; GS-0976, an ACC inhibitor, GS-9674, an FXR agonist, and selonsertib, an ASK1 inhibitor, from Gilead; OCA from Intercept; MGL-3196, a beta-thyroid hormone receptor agonist from Madrigal; pegbelfermin, a PEGylated FGF21, from Bristol-Myers Squibb; elobixibat, an IBAT-inhibitor from Albireo; a Galectin-3 inhibitor from Galectin; a synthetic conjugate of cholic acid and arachidic acid from Galmed; an FXR agonist from Metacrine; FXR agonists from Novartis; a mitochondrial pyruvate complex modulator from Cirius; and a PPAR alpha/delta agonist from Genfit. In addition, a NDA for OCA was filed with the FDA in September 2019 and the completion of their review is expected in June 2020. The foregoing competitive risks apply to aldafermin and NGM313 and any variants of aldafermin and NGM313 we may commercialize, including the second-generation, half-life extended version of FGF19 we are currently developing.

If NGM395 is approved for the treatment of obesity, it would face competition from currently approved and marketed products, including *Saxenda* (liraglutide), *Contrave* (bupropion and naltrexone), *Qsymia* (phentermine and topiramate extended-release), *Belviq* (lorcaserin HCL) and *Xenical* (orlistat). Further competition could arise from products currently in development, including Lilly's tirzepatide (dual GLP-1/GIP receptor agonist). To the extent any of our product candidates are approved for cardio-metabolic indications, particularly obesity, the commercial success of our products will also depend on our ability to demonstrate benefits over the then-prevailing standard of care, including diet and exercise. Finally, morbidly obese patients sometimes undergo the gastric bypass procedure, with salutary effects on the many co-morbid conditions of obesity. Some of these programs have been advanced further in clinical development than our clinical programs or have already received regulatory approval.

If any of our product candidates is approved for the treatment of type 2 diabetes, these products would face competition from currently approved and marketed products, including: biguanides; sulfonylureas; TZDs; alpha-glucosidase inhibitors (AGIs); dipeptidyl peptidase 4 (DPP4) inhibitors; glucagon-like peptide-1 (GLP-1) analogues; SGLT2 inhibitors; oral GLP-1 mimetics; and insulins, including injectable and inhaled versions. Further competition could arise from products currently in development, including: 11 beta HSD (Incyte, Japan Tobacco, Roche); and GPR40 (Connexios, Takeda). Some of these programs have been advanced further in clinical development than our product candidates and could receive approval before our product candidates are approved, if they are approved at all.

Manufacturing

We currently use third-party manufacturers to manufacture clinical quantities of aldafermin, NGM120, NGM217, NGM621 and NGM395. As we advance our product candidates through clinical development and greater quantities of our biological molecules are required, we plan to continue to use third parties to manufacture our product candidates.

We also plan to rely on third parties to manufacture commercial quantities of any products we successfully develop. Among the conditions for FDA approval of a pharmaceutical product is the requirement that the manufacturer's quality control and manufacturing procedures conform to cGMP, which must be followed at all times. The FDA typically inspects manufacturing facilities every two years. In complying with cGMP regulations, pharmaceutical manufacturers must expend resources and time to ensure compliance with product specifications as well as production, record keeping, quality control, reporting and other requirements.

Sales and Marketing

We currently have no marketing, sales or distribution capabilities. In order to commercialize any products outside of our existing collaboration that are approved for commercial sale, we must either develop a sales and marketing infrastructure or collaborate with third parties that have sales and marketing experience.

We may elect to establish our own sales force to market and sell a product for which we obtain regulatory approval if we elect to exercise our co-detail option on a product candidate from our collaboration with Merck or if we expect that the geographic market for a product we develop on our own is limited or that the prescriptions for the product will be written principally by a relatively small number of physicians. If we decide to market and sell any products ourselves, we do not expect to establish direct sales capability until shortly before the products are approved for commercial sale, if they are approved at all.

We plan to seek third-party support from established pharmaceutical and biotechnology companies, such as Merck, for those products that would benefit from the promotional support of a large sales and marketing force. In these cases, we might seek to promote our products in collaboration with marketing partners or rely on relationships with one or more companies with large established sales forces and distribution systems.

Intellectual Property

Our success depends, in part, on our ability to obtain and maintain intellectual property protection for our product candidates, technology and know-how, to defend and enforce our intellectual property rights, in particular, our patent rights, to preserve the confidentiality of our trade secrets and to operate without infringing the proprietary rights of others. We seek to protect our biological molecules and technologies by, among other methods, filing U.S. and foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development of our business, where patent protection is available. We also rely on trade secrets, know-how, continuing technological innovation and in-licensing of third-party intellectual property to develop and maintain our proprietary position. We, or Merck, which we sometimes refer to as our collaborator, file patent applications directed to our key product candidates in an effort to establish intellectual property positions regarding new biological molecules relating to our product candidates as well as uses of our product candidates and/or new biological molecules for the treatment of diseases.

Licensing Arrangements

Horizon License

In September 2019, we entered into a license agreement with Horizon Discovery Ltd. ("Horizon"), a United Kingdom-based company, in which we obtained a non-exclusive, non-transferable and non-sub-licensable license to use their proprietary GS knockout CHO K1 manufacturing cell line ("Horizon License"). The Horizon License will continue for ten years and allow us to manufacture and commercialize any current or future product candidates within the contractual term, including our product candidates that are currently subject to our collaboration with Merck.

Pursuant to the Horizon License, we paid Horizon a one-time, non-creditable and non-refundable license fee of $1.2 million, of which 50% of the license fee was reimbursed by Merck. We are also subject to a license fee of $0.2 million for each future strategic partner. We have the right to terminate the Horizon License upon written notice to Horizon and each party may also terminate the Horizon License in the event of the other party's uncured material breach.

Lonza License

In October 2014, we entered into a Multi-Product License Agreement (the "Lonza License") with Lonza Sales AG ("Lonza"), under which we obtained a worldwide, non-exclusive license to use Lonza's glutamine synthetase gene expression system, known as GS Xceed™, to manufacture and commercialize our proprietary products, including our product candidates that are currently subject to our collaboration with Merck.

Pursuant to the Lonza License, we paid Lonza an upfront fee of £250,000. Upon the initiation of the first phase 2 clinical trial, the first phase 3 clinical trial and the first commercial sale of any product manufactured using GS Xceed™, we are required to pay Lonza one-time milestone payments of £100,000, £100,000 and £150,000, respectively. We are also required to pay low single-digit royalties to Lonza based on net sales of any product manufactured using GS Xceed™. Our royalty obligation to Lonza continues on a product-by-product basis until the later of the expiration of the last-to-expire licensed patent or ten years after the first commercial sale of the product. We are also required to pay an annual license fee to Lonza of up to £300,000 per product if a party other than Lonza, we, our affiliates or our strategic partners (including Merck) manufactures the product for commercial activities. We are currently required to pay this fee for NGM313, NGM120, NGM217 and NGM395. In accordance with the Lonza License amendment, for any additional product candidates, we are required to pay an annual license fee to Lonza of £25,000 per product prior to the initiation of clinical development and £100,000, £150,000 and £300,000 per product, respectively, if such product is in a Phase 1, Phase 2 and Phase 3 clinical trial. We are currently required to pay this fee for NGM621 and any future product candidates utilizing this license.

The Lonza License continues until the expiration of the royalty term. We have the right to terminate the Lonza License upon written notice to Lonza. Each party may terminate the Lonza License for the other party's uncured material breach or bankruptcy. In addition, Lonza may terminate the Lonza License if we participate in the opposition or challenge of any Lonza patent or patent application licensed to us under the Lonza License.

Patents and Other Proprietary Rights

As of January 31, 2020, we owned 37 issued U.S. patents and 38 pending U.S. patent applications (seven of which are provisional applications) along with 39 granted patents and approximately 203 corresponding patent applications in foreign jurisdictions (six of which are Patent Cooperation Treaty ("PCT") applications), associated with, for example, the treatment of, cardio-metabolic, liver, ophthalmic and bile acid-related diseases. The issued patents and pending patent applications contain claims directed to various aspects of our work, including compositions of matter, methods of treatment, use of our product candidates in combination with certain other therapeutics and formulations.

Aldafermin Patent Portfolio

Our aldafermin product candidate, and related compositions-of-matter and methods of use, are covered by 21 U.S. patents, as well as issued patents in the following foreign countries: Australia, Japan, Malaysia, Mexico, New Zealand, Peru, Philippines, Russia, Ukraine, South Africa and various member states of the European Patent Office ("EPO") including Germany, France, Italy, Spain and the United Kingdom; and are disclosed and claimed in other applications that are pending in the United States and the following foreign countries and regions: Australia, Brazil, Canada, Chile, China, Egypt, the EPO, Hong Kong, India, Indonesia, Israel, Japan, Republic of Korea, Mexico, New Zealand, Singapore, South Africa, United Arab Emirates and Vietnam. The earliest expected expiration date for these patents and any patents issuing from these patent applications is June 2032, exclusive of possible patent term extensions or adjustments. Any changes we make to the aldafermin molecule to cause it to have what we view as more advantageous properties may not be covered by our existing patents and patent applications, and we may be required to file new applications and/or seek other forms of protection for any such altered molecule. The patent landscape surrounding FGF19, the naturally occurring hormone upon which aldafermin is based, is crowded, and there can be no assurance that our pending patent applications will be issued with the claims we are seeking or that we would be able to secure patent protection that would adequately cover an alternative to our aldafermin molecule, including the half-life extended variant of FGF19 that we are developing, nor can there be any assurance that we will obtain sufficiently broad claims to be able to prevent others from selling competing products.

NGM313 Patent Portfolio

Our NGM313 product candidate, and related compositions-of-matter and methods of use, are covered by two issued U.S. patents and issued patents in Colombia, Russia, and Ukraine; and are disclosed and claimed in other applications that are pending in the United States and the following foreign countries and regions: Australia, Brazil, Canada, Chile, China, the EPO, Hong Kong, India, Indonesia, Israel, Japan, Republic of Korea, Malaysia, Mexico, New Zealand, Peru, Philippines, Singapore, South Africa and Vietnam. The earliest expected expiration date for these patents and any patents issuing from these patent applications is January 2035, exclusive of possible patent term extensions or adjustments. Any changes we make to the NGM313 molecule to cause it to have what we view as more advantageous properties may not be covered by our existing patents and patent applications, and we may be required to file new applications and/or seek other forms of protection for any such altered molecule. The patent landscape surrounding antibodies to FGFR1c/KLB is crowded, and there can be no assurance that our pending patent applications will be issued with the claims we are seeking or that we would be able to secure patent protection that would adequately cover an alternative to our NGM313 molecule, nor can there be any assurance that we will obtain sufficiently broad claims to be able to prevent others from selling competing products.

NGM120 Patent Portfolio

Our NGM120 product candidate, and related compositions-of-matter and methods of use, are disclosed and claimed in one issued U.S. patent and in applications pending in the following foreign countries and regions: Australia, Brazil, Canada, Chile, China, Colombia, Egypt, the EPO, India, Indonesia, Israel, Japan, Republic of Korea, Malaysia, Mexico, New Zealand, Peru, Philippines, Russian Federation, Singapore, South Africa, Taiwan R.O.C., Ukraine and Vietnam. The earliest expected expiration date for this patent and any patents issuing from these patent applications is October 2037, exclusive of possible patent term extensions or adjustments. Any changes we make to the NGM120 molecule to cause it to have what we view as more advantageous properties may not be covered by our existing patent and patent applications, and we may be required to file new applications and/or seek other forms of protection for any such altered molecule. The patent landscape surrounding antibodies to GFRAL is crowded, and there can be no assurance that our pending patent applications will be issued with the claims we are seeking or that we would be able to secure patent protection that would adequately cover an alternative to our NGM120 molecule, nor can there be any assurance that we will obtain sufficiently broad claims to be able to prevent others from selling competing products.

NGM217 Patent Portfolio

We do not currently own or have a license to any issued patent that covers our NGM217 product candidate. However, our NGM217 product candidate, and related compositions-of matter and methods of use, are disclosed and claimed in pending United States and PCT applications and in applications pending in the following foreign countries and regions: Australia, Brazil, Canada, Chile, China, Colombia, the EPO, India, Indonesia, Israel, Japan, Republic of Korea, Malaysia, Mexico, New Zealand, Peru, Philippines, Russian Federation, Singapore, South Africa, Ukraine and Vietnam. The earliest expected expiration date for any patents issuing from these patent applications is January 2038, exclusive of possible patent term extensions or adjustments. Any changes we make to the NGM217 molecule to cause it to have what we view as more advantageous properties may not be covered by our existing patent applications, and we may be required to file new applications and/or seek other forms of protection for any such altered molecule. There can be no assurance that our pending patent applications will be issued with the claims we are seeking or that we would be able to secure patent protection that would adequately cover an alternative to our NGM217 molecule, nor can there be any assurance that we will obtain sufficiently broad claims to be able to prevent others from selling competing products.

NGM621 Patent Portfolio

We do not currently own or have a license to any issued patent that covers our NGM621 product candidate. However, our NGM621 product candidate, and related compositions-of-matter and methods of use, are disclosed and claimed in a pending United States provisional application filed in April 2018 that we expect to use as the basis for U.S. non-provisional and PCT applications, and in applications pending in the following foreign countries and regions: Argentina and Taiwan R.O.C.. Any changes we make to the NGM621 molecule to cause it to have what we view as more advantageous properties may not be covered by our existing patent applications, and we may be required to file new applications and/or seek other forms of protection for any such altered molecule. There can be no assurance that our pending patent applications will be issued with the claims we are seeking or that we would be able to secure patent protection that would adequately cover an alternative to our NGM621 molecule, nor can there be any assurance that we will obtain sufficiently broad claims to be able to prevent others from selling competing products.

NGM395 Patent Portfolio

Our NGM395 product candidate, and related compositions-of-matter and methods of use, are covered by one issued U.S. patent as well as issued patents in Columbia and Mexico; and are disclosed and claimed in other applications that are pending in the United States and the following foreign countries and regions: Argentina, Australia, Brazil, Canada, Chile, China, Colombia, Ecuador, Egypt, the Eurasian Patent Office, the EPO, Gulf Cooperation Council, Hong Kong, India, Indonesia, Israel, Jamaica, Japan, Jordan, Republic of Korea, Malaysia, Mexico, New Zealand, Peru, Philippines, Singapore, South Africa, Taiwan R.O.C., Thailand, Ukraine, Venezuela and Vietnam. The earliest expected expiration date for these patents and any patents issuing from these patent applications is October 2035, exclusive of possible patent term extensions or adjustments. Any changes we make to the NGM395 molecule to cause it to have what we view as more advantageous properties may not be covered by our existing patents and patent applications, and we may be required to file new applications and/or seek other forms of protection for any such altered molecule. The patent landscape surrounding GDF15, the naturally occurring hormone upon which NGM395 is based, is crowded, and there can be no assurance that our pending patent applications will be issued with the claims we are seeking or that we would be able to secure patent protection that would adequately cover an alternative to our NGM395 molecule, nor can there be any assurance that we will obtain sufficiently broad claims to be able to prevent others from selling competing products.

The actual term of any patent that may issue from the above-described patent applications claiming one of our product candidates could be longer than described above due to patent term adjustment or patent term extension, if available, or shorter if we are required to file terminal disclaimers. The term of individual patents depends upon the legal term for patents in the countries in which they are granted. In most countries, including the United States, the patent term is 20 years from the earliest claimed filing date of a non-provisional patent application in the applicable country.

The U.S. patent system permits the filing of provisional and non-provisional patent applications. A provisional patent application is not examined for patentability by the U.S. Patent and Trademark Office (“USPTO”), and automatically expires 12 months after its filing date. As a result, a provisional patent application cannot mature into an issued patent. Provisional applications are often used, among other things, to establish an early effective filing date for a later-filed non-provisional patent application. A non-provisional patent application is examined by the USPTO and can mature into a patent once the USPTO determines that the claimed invention meets the standards for patentability. If we do not timely file any non-provisional patent applications with respect to any of our provisional patent applications, we may lose the ability to claim benefit of the provisional application filing date with respect to the inventions disclosed therein. While we intend to timely file non-provisional patent applications relating to our provisional patent applications, we cannot predict whether any such patent applications will result in the issuance of patents that provide us with any competitive advantage.

Our ability to maintain and solidify our proprietary position for our product candidates and technology will depend on our success in obtaining effective patent claims and enforcing those claims once granted. We do not know whether any of our patent applications will result in the issuance of any patents, or what the scope of the claims in any future issued patents may be. Our issued patents and those that may issue in the future, or those licensed to us, may be challenged, invalidated, narrowed, rendered unenforceable or circumvented, which could limit our ability to stop competitors from marketing identical or substantially similar products or could reduce the length of term of patent protection that we may have for our products. In addition, the claims granted in any of our issued patents may not provide us with advantages against competitors with similar biological molecules or technology. Furthermore, our competitors may independently develop technologies that are similar or identical to technology developed by us but that do not infringe our patents or other intellectual property. Because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that, by the time that any of our drug candidates or those developed by our collaborator can be commercialized, the key patent may have expired or may only continue to remain in force for a short period of time following commercialization, thereby reducing the usefulness of the patent.

We seek to protect our proprietary technology and processes, in part, by confidentiality agreements with our employees, consultants, scientific advisors and other contractors. These agreements may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our employees, consultants, advisors or other contractors use technology or know-how owned by others in their work for us, disputes may arise as to the rights in related inventions. For this and more comprehensive risks related to our intellectual property, see “Risk Factors—Risks Related to Our Intellectual Property.”

Employees

As of December 31, 2019, we had 186 employees. Of these employees, approximately 152 employees are engaged in research and development activities.

Corporate and Available Information

We were incorporated in Delaware in December 2007 and commenced operations in 2008. Our principal executive offices are located at 333 Oyster Point Blvd., South San Francisco, CA 94080-7014, and our telephone number is (650) 243-5555. Our website address is http://www.ngmbio.com.

We file or furnish electronically with the U.S. Securities and Exchange Commission (the “SEC”) annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act. We make copies of these reports available free of charge through our investor relations website as soon as reasonably practicable after we file or furnish them with the SEC.

Information contained on or accessible through our websites is not incorporated into, and does not form a part of, this Annual Report or any other report or document we file with the SEC, and any references to our websites are intended to be inactive textual references only.

Item 1A. Risk Factors.

Risks Related to Our Financial Results and Capital Needs

We have incurred net losses every year since our inception, expect to incur significant and increasing operating losses and may never be profitable. Our stock is a highly speculative investment.

We are a clinical-stage biopharmaceutical company that was incorporated in 2007 and commenced operations in early 2008. Investment in biopharmaceutical product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate effect and/or an acceptable safety profile, gain regulatory approval and become commercially viable. We have no products approved for commercial sale and have not generated any revenue from product sales to date, and we continue to incur significant research and development and other expenses related to our ongoing operations. As a result, we are not profitable and have incurred losses in each year since commencing operations. Our net loss was $42.8 million, $0.5 million and $14.2 million for the years ended December 31, 2019, 2018 and 2017, respectively. As of December 31, 2019, we had an accumulated deficit of $196.1 million.

We have spent, and expect to continue to spend, significant resources to fund research and development of, and seek regulatory approvals for, our product candidates. We will require substantial additional capital to achieve our development and commercialization goals for our wholly-owned programs, aldafermin and NGM395, for any future programs that Merck does not opt to license under the Collaboration Agreement and that we choose to develop, for any Merck licensed programs that we opt to co-develop, and for any programs that Merck chooses to license under the Collaboration Agreement and later elects to terminate. We expect to incur substantial and increasing operating losses over the next several years as our research, development, preclinical testing, clinical trial and related activities increase. As a result, our accumulated deficit will also increase significantly. We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue beyond those generated pursuant to the Merck collaboration. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital. Even if we eventually generate product revenue, we may never be profitable and, if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis.

Substantially all of our revenue for recent periods has been received from a single collaboration partner.

Since executing the Collaboration Agreement with Merck in 2015, substantially all of our revenue has been from our collaboration partner, Merck. Under the collaboration, Merck provides us with reimbursement for research and development activities of up to $50 million per year, plus additional amounts up to agreed upon annual caps, if certain conditions are met; however, we may require additional funding to advance our research and development affairs on our planned timeline, or at all. If our Merck collaboration were to be terminated, or if the annual cap under the Merck collaboration is insufficient, we could require significant additional capital in order to proceed with development and commercialization of our product candidates, or we may require additional partnering in order to help fund such development and commercialization. Merck has exercised its option to extend the research and early development program through March 16, 2022 and has the right to extend it again through March 16, 2024. If adequate funds or partners are not available to us on a timely basis, on favorable terms or at all, we may be required to delay, limit, reduce or terminate our research and development efforts or other operations.

We currently have no source of product revenue and may never become profitable.

Our product candidates are in the early stages of development. To date, we have not generated any revenue from commercialization of our product candidates. We will not be able to generate product revenue unless and until one of our product candidates, alone or with our partners, successfully completes clinical trials, receives regulatory approval and is successfully commercialized. As our product candidates are in early stages of development, we do not expect to receive revenue from those product candidates for a number of years, if ever. We may seek to obtain revenue from collaboration or licensing agreements with third parties. Other than our agreement with Merck, we currently have no such agreements that could provide us with material, ongoing future revenue and we may never enter into any such agreements. Our ability to generate future product revenue from our current or future product candidates also depends on a number of additional factors, including our or our current collaborator's and potential future collaborators' ability to:

- successfully complete research and clinical development of current and future product candidates;
- establish and maintain supply and manufacturing relationships with third parties, and ensure adequate and legally compliant manufacturing of bulk drug substances and drug products to maintain sufficient supply;
- launch and commercialize any product candidates for which we obtain marketing approval, if any, and, if launched independently, successfully establish a sales force, marketing and distribution infrastructure;
- demonstrate the necessary safety data post-approval to ensure continued regulatory approval;
- obtain coverage and adequate product reimbursement from third-party payors, including government payors;
- achieve market acceptance for our or our partners' products, if any;
- establish, maintain, protect and enforce our intellectual property rights; and
- attract, hire and retain qualified personnel.

In addition, because of the numerous risks and uncertainties associated with pharmaceutical product development, including that our product candidates may not advance through development or achieve the endpoints of applicable clinical trials, we are unable to predict the timing or amount of increased expenses, or if or when we will achieve or maintain profitability. In addition, our expenses could increase beyond expectations if we decide, or are required by the FDA or foreign regulatory authorities, to perform studies or trials in addition to those that we currently anticipate. Even if we complete the development and regulatory processes described above, we anticipate incurring significant costs associated with launching and commercializing these products.

Even if we generate revenue from the sale of any of our products that may be approved, we may not become profitable and may need to obtain additional funding to continue operations. If we fail to become profitable or do not sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce our operations.

We may require additional capital to finance our operations, which may not be available to us on acceptable terms, or at all. As a result, we may not complete the development and commercialization of our current product candidates or develop new product candidates.

As a research and development company, our operations have consumed substantial amounts of cash since inception. We expect our research and development expenses to increase substantially in connection with our ongoing activities, particularly to the extent that product candidates whose costs are not borne by our collaborator, such as our wholly-owned programs, aldafermin and NGM395, advance in clinical development. We believe that our existing cash, cash equivalents and short-term marketable securities and funding we expect to receive under our existing Collaboration Agreement, will fund our projected operating requirements for at least the next twelve months. Our forecast of the period of time through which our financial resources will adequately support our operations is a forward-looking statement and involves risks and uncertainties, and actual results could vary as a result of a number of factors, including the factors discussed elsewhere in this *"Risk Factors"* section. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. Our future funding requirements, both short- and long-term, will depend on many factors, including:

- the initiation, progress, timing, costs and results of preclinical tests and clinical trials for our current product candidates and any future product candidates we may develop;
- whether Merck exercises its option to license product candidates upon our completion of proof-of-concept studies for each such candidate in humans;
- whether Merck terminates the research collaboration under pre-specified circumstances set forth in the Collaboration Agreement or terminates a program that is licensed (such as Merck's termination of its license for NGM395 and NGM386);
- whether Merck exercises its remaining option to extend the research phase of its collaboration with us, which would trigger an extension payment to us;
- the outcome, timing and cost of seeking and obtaining regulatory approvals from the FDA and comparable foreign regulatory authorities, including the potential for such authorities to require that we perform more studies than those that we currently expect or to change their requirements on studies that had previously been agreed to;
- the cost to establish, maintain, expand, enforce and defend the scope of our intellectual property portfolio, including the amount and timing of any payments we may be required to make, or that we may receive, in connection with licensing, preparing, filing, prosecuting, defending and enforcing any patents or other intellectual property rights;
- the effect of products that may compete with our product candidates and market developments;
- market acceptance of any approved product candidates, including product pricing and product reimbursement by third-party payors;
- the cost of acquiring, licensing or investing in additional businesses, products, product candidates and technologies;
- the cost and timing of selecting, auditing and potentially validating a manufacturing site for commercial-scale manufacturing;
- the cost of establishing sales, marketing and distribution capabilities for our product candidates for which we may receive regulatory approval and that we determine to commercialize ourselves or in collaboration with partners; and
- the extent to which any of the foregoing costs are the responsibility of Merck.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our product candidates or intellectual property.

Unless and until we can generate a sufficient amount of revenue from approved products, we will require additional capital to discover, develop, obtain regulatory approval for and commercialize our current and future product candidates. We do not have any committed external source of funds, other than pursuant to our collaboration with Merck, which is limited in scope and duration, and may be terminated in certain circumstances. We expect to finance future cash needs through public or private equity or debt offerings or product collaborations. Additional capital may not be available in sufficient amounts or on reasonable terms, if at all, and our ability to raise additional capital may be adversely impacted by potential worsening global economic conditions and the recent disruptions to and volatility in the credit and financial markets in the United States and worldwide resulting from the ongoing COVID-19 pandemic. Our existing stockholders could suffer dilution or be negatively affected by fixed payment obligations we may incur if we raise additional funds through the issuance of additional equity securities or debt. Furthermore, these securities may have rights senior to those of our common stock and could contain covenants or protective rights that would restrict our operations and potentially impair our competitiveness, 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. If we need to secure additional financing, such additional fundraising efforts may divert our management and research efforts from our day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. If we do not raise additional capital, we may not be able to expand our operations or otherwise capitalize on our business opportunities, our business and financial condition will be negatively impacted and we may need to:

- significantly delay, scale back or discontinue research and discovery efforts and the development or commercialization of any product candidates or cease operations altogether;
- seek strategic alliances for research and development programs when we otherwise would not, or at an earlier stage than we would otherwise desire or on terms less favorable than might otherwise be available; or
- relinquish, or license on unfavorable terms, our rights to intellectual property or any product candidates that we otherwise would seek to develop or commercialize ourselves.

If we need to conduct additional fundraising activities, but are unable to do so, we may be prevented from pursuing development and commercialization efforts, which will have a material adverse effect on our business, operating results and prospects.

To the extent we obtain additional funding through product collaborations, these arrangements would generally require us to relinquish rights to some of our intellectual property, product candidates or products, and we may not be able to enter into such agreements on acceptable terms, if at all. If we are unable to obtain additional funding on a timely basis, we may be required to curtail or terminate some or all of our research and development programs or product candidates.

We plan to use current year operating losses and our federal and state net operating loss ("NOL") carryforwards to offset taxable income from revenue generated from operations, including corporate collaborations. However, our ability to use NOL carryforwards could be limited.

We plan to use our current year operating losses to offset taxable income from any revenue generated from operations, including corporate collaborations. To the extent that our taxable income exceeds any current year operating losses, we plan to use our NOL carryforwards to offset income that would otherwise be taxable. However, under Section 382 of the U.S. Internal Revenue Code of 1986, as amended, the amount of benefits from our NOL carryforwards may be impaired or limited if we incur a cumulative ownership change of more than 50%, as interpreted by the U.S. Internal Revenue Service, over a three-year period. We may have experienced ownership changes in the past and may experience ownership changes in the future as a result of our IPO and subsequent shifts in our stock ownership, some of which are outside our control. As a result, our use of federal NOL carryforwards could be limited. State NOL carryforwards may be similarly limited. Any such disallowances may result in greater tax liabilities than we would incur in the absence of such a limitation and any increased liabilities could adversely affect our business, results of operations, financial position and cash flows.

Risks Related to Our Business and Industry

Our product candidates must undergo rigorous clinical trials and regulatory approvals, which could delay or prevent commercialization of our product candidates.

All of our product candidates will be subject to rigorous and extensive clinical trials and extensive regulatory approval processes implemented by the FDA and similar regulatory bodies in other countries. The approval process is typically lengthy and expensive, and approval is never certain. Clinical trials may be delayed, suspended or terminated at any time for reasons including:

- ongoing discussions with the FDA or comparable foreign authorities regarding the scope or design of our clinical trials;
- delays in obtaining, or the inability to obtain, required approvals from IRBs or other governing entities at clinical sites selected for participation in our clinical trials;
- delays in enrolling participants into clinical trials, such as the delay in enrollment we experienced in our ALPINE 2/3 clinical trial;
- lower than anticipated retention rates of participants in clinical trials;
- implementation of new, or changes to, guidance or interpretations from the FDA or comparable foreign authorities with respect to approval pathways for product candidates we are pursuing, such as draft guidance documents from the FDA for the development of products for the treatment of NASH that issued in 2018 and 2019 and from the European Medicines Agency ("EMA") that issued in 2018;
- the need to repeat clinical trials as a result of inconclusive or negative results, poorly executed testing or changes in required endpoints by the FDA or comparable foreign authorities;
- insufficient supply or deficient quality of product candidate materials or other materials necessary to conduct our clinical trials;
- unfavorable FDA or comparable foreign authority inspection and review of a clinical trial site or records of any clinical or preclinical investigation;
- serious and unexpected drug-related adverse effects experienced by participants in our clinical trials; or
- the placement of a clinical hold on a trial by the FDA or comparable foreign authorities.

Positive or timely results from preclinical studies and early clinical trials do not ensure positive or timely results in late-stage clinical trials or product approval by the FDA or any other regulatory authority. Product candidates that show positive preclinical or early clinical results often fail in later stage clinical trials. Data obtained from preclinical and clinical activities is susceptible to varying interpretations, which could delay, limit or prevent regulatory approvals.

We have limited experience in conducting late-stage clinical trials required to obtain regulatory approval. We may not be able to conduct clinical trials at preferred sites, enlist clinical investigators, enroll sufficient numbers of participants or begin or successfully complete clinical trials in a timely fashion, if at all. Our current clinical trials may be insufficient to demonstrate that our potential products will be safe or effective. Additional clinical trials may be required if clinical trial results are negative or inconclusive, which will require us to incur additional costs and significant delays. If we do not receive the necessary regulatory approvals, we will not be able to generate product revenue and may not become profitable.

If clinical trials of our product candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we or our collaborators must conduct extensive preclinical studies and clinical trials to demonstrate the safety and efficacy of the product candidates in humans. Preclinical studies and clinical trials are expensive, take several years to complete and may not yield results that support further clinical development or product approvals. A failure of one or more clinical trials can occur at any stage of testing.

To date, the data supporting our drug discovery and development programs are derived from laboratory and preclinical studies and earlier-stage clinical trials. Despite the results reported in our Phase 1 and 2 clinical trials for aldafermin, in Phase 1 clinical trials for NGM313 and NGM120 and in preclinical studies for our other product candidates, future clinical trials in humans may show that one or more of our product candidates are not safe and effective, in which event we may need to abandon development of such product candidates. It is impossible to predict when or if any of our product candidates will prove effective or safe in humans or will receive regulatory approval. Owing in part to the complexity of biological pathways, these compounds might not demonstrate in patients the biochemical and pharmacological properties we anticipate based on laboratory studies or earlier-stage clinical trials, and they may interact with human biological systems or other drugs in unforeseen, ineffective or harmful ways.

Further, we expect that our current product candidates will, and future product candidates may, require chronic administration. The need for chronic administration increases the risk that participants in our clinical trials will fail to comply with our dosing regimens. If participants fail to comply, we may not be able to generate clinical data in our trials acceptable to the FDA or foreign regulatory authorities. The need for chronic administration also increases the risk that our clinical drug development programs may not uncover all possible adverse events that patients who take our products may eventually experience. The number of patients exposed to treatment with, and the average exposure time to, our product candidates in clinical development programs may be inadequate to detect rare adverse events or chance findings that may only be detected once our products are administered to more patients and for longer periods of time.

If we are unable to successfully discover, develop or enable our collaborators to develop drugs that are effective and safe in humans, we will not have a viable business.

Phase 2 clinical trials of aldafermin that have produced and will produce NASH histology data are ongoing, and the clinical data produced to date are preliminary and have not been subjected to quality control procedures. Preliminary data and interim results may not be predictive of final results.

We have ongoing Phase 2 clinical trials of aldafermin in NASH. Any data and results we have announced from our first Phase 2 clinical trial, including the topline results from the 24-week cohort announced in February 2020 are preliminary. Until the final data is received, we are unable to perform typical quality control procedures on the data produced to ensure its accuracy. While we believe the data made available to date are accurate, until such time as the final quality control procedures are performed, the data are and should be regarded as preliminary. Preliminary data and interim results may not be predictive of final results and may not be predictive of future results in later-stage clinical trials. Differences between the preliminary data, data from the interim analysis and final data in our aldafermin trials may lead us to make different operational decisions regarding, or incur additional expenses for, the development of aldafermin than we otherwise would if final data were available. Our business and prospects depend on the development of aldafermin and, if final data is less promising than the preliminary data suggests, our business and prospects could be adversely affected.

Success in preclinical studies or earlier-stage clinical trials may not be indicative of results in future clinical trials.

Success in preclinical studies and earlier-stage clinical trials does not ensure that later clinical trials will generate the same results or otherwise provide adequate data to demonstrate the effectiveness and safety of our product candidates. Similarly, preliminary data and interim results from clinical trials may not be predictive of final results. Frequently, product candidates that have shown promising results in early clinical trials have subsequently suffered significant setbacks in later clinical trials. To date, some of our clinical trials have involved small patient populations at single sites and, because of the small sample size in such trials, the results of these clinical trials may be subject to substantial variability and may not be indicative of either future interim results or final results. In addition, the design of a clinical trial can determine whether its results will support approval of a product, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. Because we have limited experience designing clinical trials, we may be unable to design and execute a clinical trial to support regulatory approval. In addition, there is a high failure rate for drugs and biologic products proceeding through clinical trials. In fact, many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in preclinical studies and earlier-stage clinical trials. Similarly, the outcome of preclinical studies may not predict the success of clinical trials. Moreover, data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. In addition, we may experience regulatory delays or rejections as a result of many factors, including due to changes in regulatory policy during the period of our product candidate development. Any such delays could negatively impact our business, financial condition, results of operations and prospects.

If we experience delays in clinical testing, we will be delayed in commercializing our product candidates, our costs may increase and our business may be harmed.

Conducting clinical trials for any of our drug candidates for approval in the United States requires filing an IND application and reaching agreement with the FDA on clinical protocols, finding appropriate clinical sites and clinical investigators, securing approvals for such studies from the IRB at each such site, manufacturing clinical quantities of drug candidates and supplying drug product to clinical sites. Currently, we have multiple active INDs with the FDA in the United States, including for aldafermin for NASH and PBC, for NGM621 for GA secondary to AMD and for NGM120 for treatment of solid tumors and pancreatic cancer. We also have an active Clinical Trial Authorisation in the United Kingdom from the Medicines and Healthcare Products Regulatory Agency for NGM217 for diabetes and an active Clinical Trial Notification in Australia from the Therapeutic Good Administration for NGM395 for metabolic syndrome.

We cannot guarantee that we will be able to successfully accomplish required regulatory activities or all of the other activities necessary to initiate and complete clinical trials. As a result, our preclinical studies and clinical trials may be extended, delayed or terminated, and we may be unable to obtain regulatory approvals or successfully commercialize our products. We do not know whether any of our clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Our product development costs will increase if we experience delays in clinical testing. Significant 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 would impair our ability to successfully commercialize our product candidates and may harm our business, results of operations and prospects. Events that may result in a delay or unsuccessful completion of clinical development include:

- delays in reaching agreement on acceptable terms with prospective clinical research organizations (“CROs”) and clinical trial sites;
- FDA comments on ongoing clinical trials and potential regulatory holds imposed if such comments are not adequately addressed;
- deviations from the trial protocol by clinical trial sites and investigators, or failures to conduct the trial in accordance with regulatory requirements;
- failure of third parties, such as CROs, to satisfy their contractual duties to us or meet expected deadlines;

- delays in the testing, validation, manufacturing and delivery of the product candidates or other study materials to the clinical sites;
- for clinical trials in selected patient populations, delays in identification and auditing of central or other laboratories and the transfer and validation of assays or tests to be used to identify selected patients and test any patient samples;
- delays in patient enrollment, such as the delay in enrollment we experienced in our ALPINE 2/3 clinical trial;
- delays in patients completing a trial or returning for post-treatment follow-up;
- delays caused by patients dropping out of a trial, including due to side effects or disease progression;
- demonstration of a significant adverse safety or tolerability signal limiting the utility of the product candidate;
- changes in regulatory authority recommendations or guidance regarding development of drugs for a particular indication that we are pursuing, such as draft guidance documents from the FDA for the development of NASH that issued in 2018 and 2019 and from the EMA that issued in 2018;
- withdrawal of clinical trial sites or investigators from our clinical trials for any reason, including as a result of changing standards of care or the ineligibility of a site to participate in our clinical trials; or
- changes in government regulations or administrative actions or lack of adequate funding to continue the clinical trials.

Our or our collaborators' inability to timely complete clinical development could result in additional costs to us or impair our ability to generate product revenue or development, regulatory, commercialization and sales milestone payments and royalties on product sales.

If we or our partners are unable to enroll patients in clinical trials, we will be unable to complete these trials on a timely basis.

The timely completion of clinical trials largely depends on patient enrollment. Many factors affect patient enrollment, including:

- the size and nature of the patient population;
- the number and location of clinical sites we enroll;
- delays in enrollment due to travel or quarantine policies, or other factors, related to COVID-19;
- competition with other companies for clinical sites or patients;
- the eligibility and exclusion criteria for the trial;
- the design of the clinical trial;
- inability to obtain and maintain patient consents;
- risk that enrolled participants will drop out before completion; and
- competing clinical trials and clinicians' and patients' perceptions as to the potential advantages of the drug being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating.

In particular, there is significant competition for recruiting NASH patients in clinical trials. For example, we recently announced that enrollment in our ALPINE 2/3 trial of aldafermin had been delayed beyond our initial projections. We or our partners may be unable to enroll the patients we need to complete clinical trials on a timely basis, or at all.

We may not successfully identify, develop or commercialize our product candidates.

The success of our business depends primarily upon our ability to identify and validate new therapeutic candidates, and to identify, develop and commercialize protein and antibody therapeutics. Research programs to identify new product candidates require substantial technical, financial and human resources. Our research efforts may initially show promise in discovering potential new protein and antibody therapeutics, yet fail to yield product candidates for clinical development for a number of reasons, including:

- our research methodology may not successfully identify medically-relevant protein or antibody therapeutics or potential product candidates;
- our drug discovery efforts tend to identify and select novel, untested proteins in the particular disease indication we are pursuing, which we may fail to validate after further research work;
- we may need to rely on third parties to generate protein or antibody candidates for some of our product candidate programs;
- we may encounter product manufacturing difficulties that limit yield or produce undesirable characteristics that increase the cost of manufacturing our product candidates, cause delays or make the product candidates unmarketable;
- our product candidates may cause adverse effects in patients or subjects, even after successful initial toxicology studies, which may make the product candidates unmarketable;
- our product candidates may not demonstrate a meaningful benefit to patients or subjects; and
- our partners may change their development profiles or plans for product candidates or abandon a therapeutic area, the development of a partnered product or the commercialization of any future approved partnered product.

If any of these events occur, we may be forced to abandon our development efforts for one or more programs, which could have a material adverse effect on our business, operating results and prospects and could potentially cause us to cease operations. For example, we recently decided to suspend activities related to NGM386 to focus on advancing NGM395, a long-acting GDF15 receptor agonist. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful.

We are subject to many manufacturing risks, any of which could substantially increase our costs and limit supply of our product candidates and any future products.

To date, aldafermin and our other product candidates have been manufactured by third-party manufacturers solely for preclinical studies and clinical trials. These manufacturers may not be able to scale production to the larger quantities required for large clinical trials and for commercialization. The process of manufacturing aldafermin and our other product candidates is complex, highly regulated and subject to several risks, including:

- the process of manufacturing biologics is susceptible to product loss due to contamination, equipment failure, improper installation or operation of equipment, vendor or operator error and improper storage conditions. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects and other supply disruptions. If microbial, viral or other contaminations are discovered in our products or in the manufacturing facilities in which our products are made, the manufacturing facilities may need to be closed for an extended period of time to investigate and eliminate the contamination;

- a third-party manufacturer of a product candidate subject to our collaboration with Merck may fail to qualify upon an audit by Merck;

- the manufacturing facilities in which our products are made could be adversely affected by equipment failures, labor and raw material shortages, financial difficulties of our contract manufacturers, natural disasters, power failures, local political unrest and numerous other factors; and

- any adverse developments affecting manufacturing operations for our products may result in shipment delays, inventory shortages, lot failures, product withdrawals or recalls or other interruptions in the supply of our products. We may also have to record inventory write-offs and incur other charges and expenses for products that fail to meet specifications, undertake costly remediation efforts or seek costlier manufacturing alternatives.

For example, we have entered into a Development and Manufacturing Services Agreement with Lonza for the production of Phase 3 and commercial supplies of aldafermin. If Lonza is not able to provide us with sufficient quantities of aldafermin for our clinical trials on a timely basis, or at all, whether due to production shortages or other supply interruptions resulting from the ongoing COVID-19 pandemic or otherwise, our clinical trials or regulatory approval may be delayed. Refer to the risk factor entitled *"Our business could be adversely affected by the effects of health epidemics, including the recent COVID-19 pandemic, in regions where we or third parties on which we rely have significant manufacturing facilities, concentrations of clinical trial sites or other business operations. The COVID-19 pandemic could materially affect our operations, including at our headquarters in the San Francisco Bay Area, which is currently subject to a shelter-in-place order, and at our clinical trial sites, as well as the business or operations of our manufacturers, CROs or other third parties with whom we conduct business."*

Each of our product candidates uses certain raw materials for its manufacture, such as reagents that support cell growth. Some of these materials only have a single supplier and are purchased as necessary without a long-term supply agreement in place. Any significant delay in the acquisition or decrease in the availability of these raw materials could considerably delay the manufacture of our product candidates, which could adversely impact the timing of any planned trials or the regulatory approvals of our product candidates.

The manufacture of biologic products is complex and requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of biologic products often encounter difficulties in production, particularly in scaling up and validating initial production and ensuring the avoidance of contamination. These problems include difficulties with production costs and yields, quality control, including stability of the product, quality assurance testing, operator error and shortages of qualified personnel, as well as compliance with strictly enforced federal, state and foreign regulations. We cannot assure you that any stability or other issues relating to the manufacture of our product candidates will not occur in the future.

We have limited process development capabilities and have access only to external manufacturing capabilities. We do not have, and we do not currently plan to acquire or develop, the facilities or capabilities to manufacture bulk drug substance or filled drug product for use in clinical trials or commercialization. Any delay or interruption in

the supply of clinical trial materials could delay the completion of clinical trials, increase the costs associated with maintaining clinical trial programs and, depending upon the period of delay, require us to commence new clinical trials at additional expense or terminate clinical trials completely.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval or limit the commercial profile of an approved label.

Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign regulatory authorities. Additional clinical trials may be required to evaluate the safety profile of our product candidates. Serious adverse events that were reported in the aldafermin treatment arms from our completed Phase 1 and Phase 2 clinical trials of aldafermin include: moderate dizziness, community acquired pneumonia, iron deficiency anemia, fractured finger, pneumonitis/alveolitis, acute pancreatitis, pneumonia, pleurisy, non-myocardial infarction cardiac arrest, chest pain, vertigo, headache, accelerated hypertension, kidney mass, bowel obstruction, bilirubin increase, cholangitis, progression of PSC, intervertebral discitis, rectal bleeding and post-biopsy bleeding. In our completed Phase 1 and Phase 1b clinical trials of NGM313, there were two reported serious adverse events in the NGM313 treatment arms: cholecystitis and rectal bleeding due to hemorrhoids, both of which were deemed by the investigators to be unrelated to treatment with NGM313. In our completed Phase 1 clinical trial of NGM120, there were two reported serious adverse events in the NGM120 treatment arms: renal colic and bipolar disorder, both of which were deemed by the investigators to be unrelated to treatment with NGM120.

Significant increases in serum levels of LDL cholesterol were observed in clinical trials of aldafermin in NASH and type 2 diabetes. The drug-induced changes in LDL cholesterol were brought back to baseline levels with concomitant statin use in NASH patients, however, sustained LDL cholesterol elevations in untreated patients can be associated with cardiovascular disease. While the impact of these drug-induced changes in cholesterol are unknown, we believe that concomitant statin use, along with aldafermin's triglyceride lowering and HDL cholesterol elevating properties, will provide an overall neutral to positive impact on patients' cardiovascular health. We have not observed any significant changes in LDL cholesterol with aldafermin in trials we have conducted in patients with cholestatic liver disease, such as PBC and PSC.

One subject in the aldafermin Phase 2 clinical trial in type 2 diabetes developed antibodies against aldafermin that appear to cross-react with FGF19. This patient did not demonstrate any biochemical or clinical safety concerns while in the study, and we have not identified any safety concerns while monitoring the subject following the study. Six of the 36 subjects in the aldafermin Phase 2 extension clinical trial in PBC were confirmed to have antibodies against aldafermin. These subjects have not demonstrated any biochemical or clinical safety signals that were different from observations in subjects that did not generate antibodies against aldafermin.

However, future results of our trials could reveal a high and unacceptable severity and prevalence of side effects, anti-drug antibodies or unexpected characteristics. In such an event, we could suspend or terminate our trials or the FDA or comparable foreign regulatory authorities could order us to cease clinical trials or deny approval of our product candidates for any or all targeted indications. Drug-related side effects could affect patient recruitment or the ability of enrolled subjects to complete the trial or result in potential product liability claims. Any of these occurrences could materially and adversely affect our business, financial condition and prospects.

Our most advanced clinical-stage product candidate, aldafermin, is a modified version of a human hormone that has been associated with liver cancer in rodent testing.

Aldafermin is a modified version of FGF19, a human hormone that has been associated with liver cancer in rodent testing. The IND that we filed in February 2014 for type 2 diabetes was placed on clinical hold by the FDA Division of Metabolism and Endocrinology Products pending receipt of additional information relating to the potential risk of proliferative effects of aldafermin in the livers of non-human primates and mice based on concerns relating to the observation that human FGF19 can induce hepatocellular proliferation in rodents. We withdrew this IND in January 2015, as we determined that we would not further study aldafermin in type 2 diabetes after we analyzed the results of the Phase 2 clinical trial of aldafermin in type 2 diabetes and made the determination to pursue NASH and other liver indications. To date, the FDA Division of Gastroenterology and Inborn Errors Products, which is responsible for the NASH indication, has not requested any additional information regarding the potential for aldafermin to induce hepatocellular proliferation. We have received feedback from the FDA Carcinogenicity

Assessment Committee that our preclinical data through six-month chronic toxicology studies in mice and monkeys support a single species, two-year carcinogenicity assessment in rats. The human hormone and the rodent ortholog for FGF19 share a sequence identity of approximately 50%, which means that the results of these studies of aldafermin in rats are not necessarily predictive of the potential risk of carcinogenicity in humans. To our knowledge, neither FGF19 nor any variant thereof other than aldafermin has ever been tested in humans. We believe we have identified a modified version of FGF19 that does not exhibit the cancer-causing effects of native human FGF19 in rodents. We believe that aldafermin will have a superior therapeutic profile to FGF19 based on preclinical data showing reduced fasting blood glucose levels, fed insulin levels and bile acid suppression in animals. However, we may be incorrect in these beliefs, and we cannot be sure that regulators will view our product candidate as safe or that physicians will view our product candidates as superior to alternative treatments. Concerns about the association between FGF19 and liver cancer could have an adverse effect on our ability to develop and commercialize aldafermin.

We have no experience in sales, marketing and distribution and may have to enter into agreements with third parties to perform these functions, which could prevent us from successfully commercializing our product candidates.

We currently have no sales, marketing or distribution capabilities. To commercialize our product candidates outside of the Merck collaboration, or to commercialize products subject to the Merck collaboration for which we may in the future exercise our co-detailing rights in the United States, we must either develop our own sales, marketing and distribution capabilities, which will be expensive and time consuming, or make arrangements with third parties to perform these services for us. If we exercise our co-detailing rights in the United States with respect to the Merck collaboration, we will be responsible for the costs of fielding such a sales force, subject to partial offset pursuant to the formula by which profits are allocated, and the risks of attracting, retaining, motivating and ensuring the compliance of such a sales force with the various requirements of the Merck collaboration and applicable law. If we decide to market any of our products on our own, we will have to commit significant resources to developing a marketing and sales force and supporting distribution capabilities. If we decide to enter into arrangements with third parties for performance of these services, we may find that they are not available on terms acceptable to us, or at all. If we are not able to establish and maintain successful arrangements with third parties or build our own sales and marketing infrastructure, we may not be able to commercialize our product candidates, which would adversely affect our business and financial condition.

We may fail to select or capitalize on the most scientifically, clinically and commercially promising or profitable product candidates.

We have limited technical, managerial and financial resources to determine which of our product candidates should proceed to initial clinical trials, later-stage clinical development and potential commercialization. We may make incorrect determinations in allocating resources among these product candidates. Our decisions to allocate our research and development, management and financial resources toward particular product candidates or therapeutic areas may not lead to the development of viable commercial products and may divert resources from better opportunities. Similarly, our decisions to delay or terminate drug development programs, such as our decision to suspend activities with NGM386 while we focus on NGM395, may also be incorrect and could cause us to miss valuable opportunities.

Under our Collaboration Agreement with Merck, we have the right, exercisable during a specified period prior to the commencement of Phase 3 clinical testing of the applicable product candidate, to convert our economic participation from a milestones and net sales royalty arrangement into a cost and profit share arrangement. If we exercise the cost and profit share right, we have the ability to participate in a co-detailing relationship in the United States. Due to the limited exercise period, we may have to choose whether a product candidate will be subject to a cost and profit share arrangement before we have as much information as we would like, including whether and when such program may receive FDA approval of the applicable BLA. As a result of such incomplete information or due to incorrect analysis by us, we may select a cost and profit share program that later proves to have less commercial potential than an alternative, or none at all, or may pass on a cost and profit sharing program that proves commercially successful.

We must attract and retain highly skilled employees in order to succeed. If we are not able to retain our current senior management team, especially Dr. Jin-Long Chen, and our scientific advisors or continue to attract and retain qualified scientific, technical and business personnel, our business will suffer.

To succeed, we must recruit, retain, manage and motivate qualified clinical, scientific, technical and management personnel and we face significant competition for experienced personnel. If we do not succeed in attracting and retaining qualified personnel, particularly at the management level, it could adversely affect our ability to execute our business plan and harm our operating results. We are dependent on the members of our management team and our scientific advisors for our business success. An important element of our strategy is to take advantage of the research and development expertise of our current management and to utilize the expertise of our scientific advisors in the cardio-metabolic, liver, oncologic and ophthalmic disease fields. We currently have employment letter agreements with all of our executive officers. Our employment agreements with our executive officers are terminable by them without notice and some provide for severance and change in control benefits. The loss of any one of our executive officers, including, in particular, Dr. Jin-Long Chen, our Chief Scientific Officer, or a key scientific consultant could result in a significant loss in the knowledge and experience that we, as an organization, possess and could cause significant delays, or outright failure, in the development and further commercialization of our product candidates.

To fully realize the research and development support committed under our collaboration with Merck, we will need to maintain a significant number of qualified research and development, scientific, administrative and commercial personnel. There is intense competition for qualified personnel, including management, in the technical fields in which we operate, and we may not be able to attract and retain qualified personnel necessary for the successful research, development and commercialization of our product candidates. In particular, we have experienced a very competitive hiring environment in the San Francisco Bay Area, where we are headquartered. Many of the other pharmaceutical companies that we compete against for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than we do. They also may provide more diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to high-quality candidates than what we have to offer. If we are unable to continue to attract and retain high-quality personnel, the rate and success with which we can discover and develop product candidates and our business will be limited.

Disputes under key agreements or conflicts of interest with our scientific advisors or clinical investigators could delay or prevent development or commercialization of our product candidates.

Any agreements we have or may enter into with third parties, such as collaboration, license, supplier, manufacturing, sponsored research, CRO or clinical trial agreements, may give rise to disputes regarding the rights and obligations of the parties. Disagreements could develop over contract interpretation, rights to ownership or use of intellectual property, the scope and direction of research and development, the approach for regulatory approvals or commercialization strategy. We intend to conduct research programs in a range of therapeutic areas, but our pursuit of these opportunities could result in conflicts with the other parties to these agreements that may be developing or selling pharmaceuticals or conducting other activities in these same therapeutic areas. Any disputes or commercial conflicts could lead to the termination of our agreements, delay progress of our product development programs, compromise our ability to renew agreements or obtain future agreements, lead to the loss of intellectual property rights, result in increased financial obligations for us or result in costly litigation.

We work with outside scientific advisors and collaborators at academic and other institutions that assist us in our research and development efforts. Our scientific advisors are not our employees and may have other commitments that limit their availability to us. If a conflict of interest between their work for us and their work for another entity arises, we may lose their services.

We may encounter difficulties in managing our growth, which could adversely affect our operations.

Since executing the Collaboration Agreement in 2015, we have significantly increased our headcount and advanced our pipeline and the complexity of our operations, which has placed a strain on our administrative and operational infrastructure. We expect this strain to continue as we maintain our growth and seek to obtain and manage relationships with third parties. Our ability to manage our operations and growth effectively depends upon the continual improvement of our procedures, reporting systems and operational, financial and management controls. We may not be able to expand or identify sufficiently-sized facilities to accommodate our growth, particularly given our location in South San Francisco, California and the current high demand for, and restricted supply of, research and development facilities in this market. We may not be able to implement administrative and operational improvements in an efficient or timely manner and may discover deficiencies in existing systems and controls. If we do not meet these challenges, we may be unable to take advantage of market opportunities, execute our business strategies or respond to competitive pressures, which in turn may slow our growth or give rise to inefficiencies that would increase our losses.

We may acquire additional assets, intellectual property and complementary businesses in the future. Acquisitions involve many risks, any of which could materially harm our business, including the diversion of management's attention from core business concerns, failure to effectively exploit acquired assets or intellectual property, failure to successfully integrate the acquired business or realize expected synergies or the loss of key employees from either our business or the acquired businesses.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than us.

The biopharmaceutical industry is intensely competitive and subject to rapid and significant technological change. Our competitors include multinational pharmaceutical companies, specialized biotechnology companies and universities and other research institutions. A number of pharmaceutical companies, including AbbVie, Allergan, AstraZeneca, Bayer, Boerhinger Ingelheim, Bristol-Myers Squibb, Eisai, Eli Lilly, GlaxoSmithKline, Johnson & Johnson, Merck, Novartis, Novo Nordisk, Pfizer, Roche, Sanofi and Takeda, as well as large and small biotechnology companies such as 89Bio, Akero, Albireo, Alentis, Amgen, Apellis, Ascletis, Axcella, Bird Rock, Can-Fite, Cirius, Enanta, Galectin, Galmed, Genfit, Gilead, Glympse, Immuron, Intercept, Inventiva, Iveric, Madrigal, MannKind, MediciNova, Metacrine, Mirum, Nalpropion, North Sea, Promethera, Salix, Scholar Rock, Seal Rock, Terns, Tiziana, Viking and Vivus, are pursuing the development or marketing of pharmaceuticals that target the same diseases that are targeted by our most advanced product candidates. It is probable that the number of companies seeking to develop products and therapies for the treatment of cardio-metabolic, liver, oncologic and ophthalmic diseases will increase. Many of our competitors have substantially greater financial, technical, human and other resources than we do and may be better equipped to develop, manufacture and market technologically superior products. In addition, many of these competitors have significantly greater experience than we have in undertaking preclinical testing and human clinical trials of new pharmaceutical products and in obtaining regulatory approvals of human therapeutic products. Accordingly, our competitors may succeed in obtaining FDA approval for superior products or for other products that would compete with our product candidates. Many of our competitors have established distribution channels and commercial infrastructure to support the commercialization of their products, whereas we have no such channel or capabilities. In addition, many competitors have greater name recognition and more extensive collaborative relationships. Smaller and earlier-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies.

Our competitors may obtain regulatory approval of their products more rapidly than us or may obtain patent protection or other intellectual property rights that limit our ability to develop or commercialize our product candidates. Our competitors may also develop drugs that are more effective, more convenient, more widely used and less costly or have a better safety profile than our products and these competitors may also be more successful than us in manufacturing and marketing their products. If we are unable to compete effectively against these companies, then we may not be able to commercialize our product candidates or achieve a competitive position in the market. This would adversely affect our ability to generate revenue. Our competitors also compete with us in recruiting and retaining qualified scientific, management and commercial personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

There are no currently approved therapies for NASH. Although we believe there are no approved therapies that specifically target the signaling pathways that our current product candidates are designed to modulate or inhibit, there are numerous currently approved therapies for treating the same diseases or indications, other than NASH, for which our product candidates may be useful and many of these currently approved therapies act through mechanisms similar to our product candidates. Many of these approved drugs are well-established therapies or products and are widely accepted by physicians, patients and third-party payors. Some of these drugs are branded and subject to patent protection, and others are available on a generic basis. Insurers and other third-party payors may also encourage the use of generic products or specific branded products. We expect that if our product candidates are approved, they will be priced at a significant premium over competitive generic products, including branded generic products. This may make it difficult for us to differentiate our products from currently approved therapies, which may adversely impact our business strategy. In addition, many companies are developing new therapeutics, and we cannot predict what the standard of care will be as our product candidates progress through clinical development.

If aldafermin or NGM313 were approved for the treatment of NASH, future competition could also arise from products currently in development, including: cenicriviroc, an immunomodulator that blocks CCR2 and CCR5, from Allergan; firsocostat, an ACC inhibitor, and cilofexor, an FXR agonist, both from Gilead; OCA, an FXR agonist, from Intercept; resmetirom, a beta-thyroid hormone receptor agonist, from Madrigal; pegbelfermin, PEGylated FGF21, from Bristol-Myers Squibb; AKR-001, an Fc conjugated FGF21, from Akero; elobixibat, an IBAT-inhibitor, from Albireo; a Galectin-3 inhibitor from Galectin; a synthetic conjugate of cholic acid and arachidic acid from Galmed; an FXR agonist from Metacrine; EDP-305, an FXR agonist, from Enanta; FXR agonists from Novartis; a beta-thyroid hormone receptor agonist from Viking; semaglutide, a GLP-1 analog, from Novo Nordisk; a mitochondrial pyruvate complex modulator from Cirius; and elafibranor, a PPAR alpha/delta agonist, from Genfit. The foregoing competitive risks apply to aldafermin, any variants of aldafermin, including the second-generation, half-life extended version of FGF19 we are currently developing, and NGM313.

If any of our product candidates were approved for the treatment of type 2 diabetes, these products would face competition from currently approved and marketed products, including: biguanides; sulfonylureas; TZDs; alpha-glucosidase inhibitors (AGIs); dipeptidyl peptidase 4 (DPP4) inhibitors; glucagon-like peptide-1 (GLP-1) analogues; SGLT2 inhibitors; oral GLP-1 mimetics; and insulins, including injectable and inhaled versions. Further competition could arise from products currently in development, including: 11 beta HSD (Incyte, Japan Tobacco, Roche); and GPR40 (Connexios, Takeda). Some of these programs have advanced further in clinical development than our product candidates and could receive approval before our product candidates are approved, if they are approved at all.

Our product candidates may not achieve adequate market acceptance among physicians, patients, healthcare payors and others in the medical community necessary for commercial success.

Even if our product candidates receive regulatory approval, they may not gain adequate market acceptance among physicians, patients, healthcare payors, pharmaceutical companies and others in the medical community. Demonstrating the safety and efficacy of our product candidates and obtaining regulatory approvals will not guarantee future revenue. Our commercial success also depends on coverage and adequate reimbursement of our product candidates by third-party payors, including government payors, which may be difficult or time-consuming to obtain, may be limited in scope and may not be obtained in all jurisdictions in which we may seek to market our products. Governments and private insurers closely examine medical products to determine whether they should be covered by reimbursement and, if so, the level of reimbursement that will apply. We cannot be certain that third-party payors will sufficiently reimburse sales of our products, or otherwise enable us to sell our products at profitable prices. Similar concerns could also limit the reimbursement amounts that health insurers or government agencies in other countries are prepared to pay for our products. In many regions, including Europe, Japan and Canada, where we may market our products, either directly or with collaborators, the pricing of prescription drugs is controlled by the government or regulatory agencies. Regulatory agencies in these countries could determine that the pricing for our products should be based on prices of other commercially available drugs for the same disease, rather than allowing us to market our products at a premium as new drugs. The degree of market acceptance of any of our approved product candidates will depend on a number of factors, including:

- the efficacy and safety profile of the product candidate as demonstrated in clinical trials;
- the timing of market introduction of the product candidate, as well as competitive products;

- the clinical indications for which the product candidate is approved;
- acceptance of the product candidate as a safe and effective treatment by clinics and patients;
- the potential and perceived advantages of the product candidate over alternative treatments, including any similar generic treatments;
- the cost of treatment in relation to alternative treatments;
- the availability of coverage and adequate reimbursement and pricing by third parties and government authorities;
- the relative convenience and ease of administration;
- the frequency and severity of adverse events;
- the effectiveness of sales and marketing efforts; and
- unfavorable publicity relating to the product candidate.

Sales of medical products also depend on the willingness of physicians to prescribe the treatment, which is likely to be based on a determination by these physicians that the products are safe, therapeutically effective and cost effective. In addition, the inclusion or exclusion of products from treatment guidelines established by various physician groups and the viewpoints of influential physicians can affect the willingness of other physicians to prescribe the treatment. We cannot predict whether physicians, physicians' organizations, hospitals, other healthcare providers, government agencies or private insurers will determine that our products are safe, therapeutically effective and cost effective as compared with competing treatments. If any product candidate is approved but does not achieve an adequate level of acceptance by such parties, we may not generate or derive sufficient revenue from that product candidate and may not become or remain profitable.

Even if we commercialize any of our product candidates, alone or with our partners, these products may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, which could harm our business.

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

Our ability to commercialize any products successfully also will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, determine which medications they will cover and establish reimbursement levels. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. The HHS department is considering new regulations that would tie certain drug payments to an International Price Index comprised of prices for the same drugs in developed countries. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that coverage and reimbursement will be available for any product that we or our partners commercialize and, if reimbursement is available, what the level of reimbursement

will be. Coverage and reimbursement may impact the demand for, or the price of, any product candidate for which we or our partners obtain marketing approval. If coverage and reimbursement are not available or reimbursement is available only to limited levels, we and our partners may not be able to successfully commercialize any product candidate for which marketing approval is obtained.

There may be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for coverage and reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including costs of research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may only be temporary. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Our inability to promptly obtain coverage and profitable reimbursement rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

The advancement of healthcare reform may negatively impact our ability to profitably sell our product candidates, if approved.

Third-party payors, whether domestic or foreign, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. The United States and many foreign jurisdictions have enacted or proposed legislative and regulatory changes affecting the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product for which we obtain marketing approval.

In March 2010, the ACA was enacted, which includes measures that have significantly changed the way health care is financed by both governmental and private insurers. Some of the provisions of the ACA have yet to be implemented, and there have been judicial and congressional challenges to certain aspects of the ACA. For example, in 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers or manufacturers of pharmaceuticals or medical devices.

In addition, while Congress has not passed comprehensive legislation repealing the ACA, it has introduced legislation to modify certain provisions. Congress will likely consider other legislation to modify or replace additional elements of the ACA. It is unclear how these efforts to repeal and replace the ACA, or other appeals, will impact the ACA and our business.

Other legislative changes that have affected or may affect our industry include the Budget Control Act of 2011 which has triggered automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of, on average, 2% per fiscal year through 2027 unless Congress takes additional action. Recently, there has also been increasing legislative and enforcement interest in the United States with respect to drug pricing practices. Specifically, there have been several recent U.S. congressional inquiries and proposed bills designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies for drugs. For example, the Trump administration released a “Blueprint” to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase drug 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. We expect that the healthcare reform measures that have been adopted and may be adopted in the future, may result in more rigorous coverage criteria and additional downward pressure on the price that we receive for any approved product and could seriously harm our future revenues. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in

payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products.

There have been, and likely will continue to be, legislative and regulatory proposals at the foreign, federal and state levels directed at broadening the availability of healthcare and containing or lowering the cost of healthcare. Such reforms could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop product candidates.

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

Our business is subject to risks associated with conducting business internationally. Some of our suppliers and clinical trial sites are located outside of the United States. Furthermore, if we, Merck or any future collaborator succeeds in developing any of our product candidates, we intend to market them in the EU and other jurisdictions in addition to the United States. If approved, we, Merck or any future collaborator may hire sales representatives and conduct physician and patient association outreach activities outside of the United States. Doing business internationally involves a number of challenges and 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;
- rejection or qualification of foreign clinical trial data by the competent authorities of other countries;
- delays or interruptions in the supply of clinical trial materials resulting from any events affecting raw material supply or manufacturing capabilities abroad, including those that may result from the ongoing COVID-19 pandemic;
- additional potentially relevant third-party patent rights;
- complexities and difficulties in obtaining, maintaining, protecting and enforcing our intellectual property;
- 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 longer payment cycles, difficulty collecting accounts receivable, the impact of local and regional financial crises on demand and payment for our products and exposure to foreign currency exchange rate fluctuations;
- natural disasters, political and economic instability, including wars, terrorism and political unrest, outbreak of disease, including COVID-19 and related shelter-in-place orders, travel, social distancing and quarantine policies, boycotts, curtailment of trade and other business restrictions;
- certain expenses, including, among others, expenses for travel, translation and insurance; and
- regulatory and compliance risks that relate to anti-corruption compliance and record-keeping that may fall within the purview of the U.S. Foreign Corrupt Practices Act, its accounting provisions or its anti-bribery provisions or provisions of anti-corruption or anti-bribery laws in other countries.

Any of these factors could harm our ongoing international clinical operations and supply chain, as well as any future international expansion and operations and, consequently, our business, financial condition, prospects and results of operations.

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

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we or our collaborator commercializes any resulting products. Product liability claims may be brought against us by subjects enrolled in our clinical trials, patients, healthcare providers or others using, administering or selling our products. If we cannot successfully defend ourselves against claims that our product candidates or products that we may develop 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 products that we may develop;
- termination of clinical trial sites or entire trial programs;
- 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 subjects or patients;
- loss of revenue;
- diversion of management and scientific resources from our business operations; and
- the inability to commercialize any products that we may develop.

Our clinical trial liability insurance coverage may not adequately cover all liabilities that we may incur. 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 inability to obtain product liability insurance at an acceptable cost or to otherwise protect against potential product liability claims could prevent or delay the commercialization of any products or product candidates that we develop. We intend to expand our insurance coverage for products to include the sale of commercial products if we obtain marketing approval for our product candidates in development, but we may be unable to obtain commercially reasonable product liability insurance for any products approved for marketing. Large judgments have been awarded in class action lawsuits based on drugs that had unanticipated side effects. If we are sued for any injury caused by our products, product candidates or processes, our liability could exceed our product liability insurance coverage and our total assets. Claims against us, regardless of their merit or potential outcome, may also generate negative publicity or hurt our ability to obtain physician endorsement of our products or expand our business.

Our relationships with healthcare providers, customers and third-party payors will be subject to applicable anti-kickback, fraud and abuse, transparency and other healthcare laws and regulations, which, if violated, could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, administrative burdens and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any product candidates for which we or our collaborator obtains marketing approval. Our arrangements with healthcare providers, third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we research, market, sell and distribute our products for which we or our collaborator obtains marketing approval. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the federal Anti-Kickback Statute prohibits persons from, among other things, knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce

or reward, or in return for, the referral of an individual for the furnishing or arranging for the furnishing, or the purchase, lease or order, or arranging for or recommending purchase, lease or order, of any good or service for which payment may be made under a federal healthcare program, such as Medicare and Medicaid;

- the federal FCA imposes criminal and civil penalties, including through civil whistleblower or *qui tam* actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;

- the federal HIPAA imposes criminal liability for knowingly and willfully executing a scheme to defraud any healthcare benefit program, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense or knowingly and willfully making false statements relating to healthcare matters;

- HIPAA, as amended by the HITECH of 2009 and its implementing regulations, also imposes obligations on certain covered entity healthcare providers, health plans and healthcare clearinghouses, as well as their business associates that perform certain services involving the use or disclosure of individually identifiable health information, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- the federal Open Payments program, created under Section 6002 of the ACA and its implementing regulations, requires manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to the HHS information related to "payments or other transfers of value" made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals and applicable manufacturers and applicable group purchasing organizations to report annually to the HHS ownership and investment interests held by physicians (as defined above) and their immediate family members; and

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; state and foreign laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers; state and local laws requiring the registration of pharmaceutical sales representatives; state and foreign laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers, marketing expenditures or pricing; and state and foreign laws that govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

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 interpreting applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, additional regulatory oversight, imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, that person or entity may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Our operations are vulnerable to interruption by fire, earthquake, power loss, telecommunications failure, terrorist activity and other events beyond our control, which could harm our business.

Our former facility was subject to electrical blackouts as a result of a shortage of available electrical power. Future blackouts, which may be implemented by the local electricity provider in the face of high winds and dry conditions, could disrupt the operations of our current facility. Our facility is located in a seismically active region. We have not undertaken a systematic analysis of the potential consequences to our business and financial results from a major earthquake, fire, power loss, terrorist activity or other disasters and do not have a complete recovery plan for such disasters. In addition, we do not carry sufficient insurance to compensate us for actual losses from interruption of our business that may occur, and any losses or damages incurred by us could harm our business. The contract manufacturing organization ("CMO") that is the sole supplier of clinical drug substance of NGM313, NGM120, NGM217, NGM621 and NGM395 is located in a region that has experienced recent political unrest.

Our business could be adversely affected by the effects of health epidemics, including the recent COVID-19 pandemic, in regions where we or third parties on which we rely have significant manufacturing facilities, concentrations of clinical trial sites or other business operations. The COVID-19 pandemic could materially affect our operations, including at our headquarters in the San Francisco Bay Area, which is currently subject to a shelter-in-place order, and at our clinical trial sites, as well as the business or operations of our manufacturers, CROs or other third parties with whom we conduct business.

Our business could be adversely affected by health epidemics in regions where we have concentrations of clinical trial sites or other business operations, and could cause significant disruption in the operations of third-party manufacturers and CROs upon whom we rely. For example, in December 2019, a novel strain of coronavirus, SARS-CoV-2, causing a disease referred to as COVID-19, was reported to have surfaced in Wuhan, China. Since then, COVID-19 has spread to multiple countries, including the United States and several European countries. Our headquarters is located in the San Francisco Bay Area, and our contract manufacturer for aldafermin, Lonza, is located in Switzerland. In March 2020, the World Health Organization declared the COVID-19 outbreak a pandemic, and the U.S. government imposed travel restrictions on travel between the United States, Europe and certain other countries. Further, the President of the United States declared the COVID-19 pandemic a national emergency, invoking powers under the Stafford Act, the legislation that directs federal emergency disaster response. Similarly, the State of California declared a state of emergency related to the spread of COVID-19, and the San Francisco Department of Public Health announced aggressive recommendations to reduce the spread of the disease. On March 16, 2020, the health officers of six San Francisco Bay Area counties, including San Mateo County where our headquarters are located, issued shelter-in-place orders, which (i) direct all individuals living in those counties to shelter at their places of residence (subject to limited exceptions), (ii) direct all businesses and governmental agencies to cease non-essential operations at physical locations in those counties, (iii) prohibit all non-essential gatherings of any number of individuals, and (iv) order cessation of all non-essential travel. The shelter-in-place orders took effect on March 17, 2020 and will continue until April 7, 2020, unless further extended. In addition, we have implemented work-from-home policies for certain employees. The effects of the shelter-in-place order and our work-from-home policies may negatively impact productivity, disrupt our business and delay our clinical programs and timelines, the magnitude of which will depend, in part, on the length and severity of the restrictions and other limitations on our ability to conduct our business in the ordinary course. These and similar, and perhaps more severe, disruptions in our operations could negatively impact our business, operating results and financial condition.

Quarantines, shelter-in-place and similar government orders, or the perception that such orders, shutdowns or other restrictions on the conduct of business operations could occur, related to COVID-19 or other infectious diseases could impact personnel at third-party manufacturing facilities in the United States and other countries, or the availability or cost of materials, which would disrupt our supply chain. In particular, some of our suppliers of certain materials used in the production of our drug products are located in Europe. For example, any manufacturing supply interruption of aldafermin, which is currently manufactured by Lonza at facilities in Switzerland, or our other product candidates, which are currently manufactured at a facility in Lithuania, could adversely affect our ability to conduct ongoing and future clinical trials of aldafermin and our other product candidates.

In addition, our clinical trials may be affected by the COVID-19 pandemic. Clinical site initiation and patient enrollment may be delayed due to prioritization of hospital resources toward the COVID-19 pandemic. Some patients may not be able to comply with clinical trial protocols if quarantines impede patient movement or interrupt

healthcare services. Similarly, our ability to recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19 and adversely impact our clinical trial operations.

The spread of COVID-19, which has caused a broad impact globally, may materially affect us economically. While the potential economic impact brought by, and the duration of, COVID-19 may be difficult to assess or predict, a widespread pandemic could result in significant disruption of global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity. In addition, a recession or market correction resulting from the spread of COVID-19 could materially affect our business and the value of our common stock.

The global pandemic of COVID-19 continues to rapidly evolve. The ultimate impact of the COVID-19 pandemic or a similar health epidemic is highly uncertain and subject to change. We do not yet know the full extent of potential delays or impacts on our business, our clinical trials, healthcare systems or the global economy as a whole. However, these effects could have a material impact on our operations, and we will continue to monitor the COVID-19 situation closely.

Our internal computer systems, or those used by our CROs or other contractors or consultants, may fail or suffer security breaches.

Similar to other companies in our industry, we face substantial cybersecurity risk. Despite the implementation of security measures, our internal computer systems and those of our current and future CROs and other contractors, collaborators and consultants may fail and are vulnerable to damage from computer viruses and unauthorized access. While we have not, to our knowledge, experienced any such material system failure 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 development programs and our business operations. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on third parties for the manufacture of our product candidates, to analyze clinical trial samples and to conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. In 2017, a security breach of the internal computer systems of our collaborator, Merck, caused material damage to its operations, but did not affect our internal operations. In June 2019, a vendor that conducted bioanalytical services for some of our aldafermin clinical trials was affected by a ransomware attack that resulted in a significant disruption to its IT systems. This cybersecurity incident at our vendor did not result in an integrity loss of certain clinical sample data for aldafermin, as verified by independent vendors. However, to the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur material costs, be exposed to liability, our competitive position could be harmed and the further development and commercialization of our product candidates could be hindered or delayed.

European data collection is governed by restrictive regulations governing the collection, use, processing and cross-border transfer of personal information.

We may collect, process, use or transfer personal information from individuals located in the EU in connection with our business, including in connection with conducting clinical trials in the EU. Additionally, if any of our product candidates are approved, we may seek to commercialize those products in the EU. The collection and use of personal health data in the EU are governed by the provisions of the General Data Protection Regulation ((EU) 2016/679) (“GDPR”). This legislation imposes requirements relating to having legal bases for processing personal information relating to identifiable individuals and transferring such information outside of the European Economic Area, including to the United States, providing details to those individuals regarding the processing of their personal information, keeping personal information secure, having data processing agreements with third parties who process personal information, responding to individuals’ requests to exercise their rights in respect of their personal information, reporting security breaches involving personal data to the competent national data protection authority and affected individuals, appointing data protection officers, conducting data protection impact assessments and record-keeping. The GDPR imposes additional responsibilities and liabilities in relation to personal data that we process and we may be required to put in place additional mechanisms ensuring compliance with the new data protection rules. Failure to comply with the requirements of the GDPR and related national data protection laws of the member states of the EU may result in substantial fines, other administrative

penalties and civil claims being brought against us, which could have a material adverse effect on our business, financial condition and results of operations.

We use and generate materials that may expose us to material liability.

Our research programs involve the use of hazardous materials, chemicals and radioactive and biological materials. We are subject to foreign, federal, state and local environmental and health and safety laws and regulations governing, among other matters, the use, manufacture, handling, storage and disposal of hazardous materials and waste products. We may incur significant costs to comply with these current or future environmental and health and safety laws and regulations. In addition, we cannot completely eliminate the risk of contamination or injury from hazardous materials and may incur material liability as a result of such contamination or injury. In the event of an accident, an injured party may seek to hold us liable for any damages that result. Any liability could exceed the limits or fall outside the coverage of our workers' compensation, property and business interruption insurance and we may not be able to maintain insurance on acceptable terms, if at all. We currently carry no insurance specifically covering environmental claims.

Risks Related to Our Dependence on Merck and Other Third Parties

We depend on our collaboration with Merck and may depend in the future on collaborations with additional third parties for the development and commercialization of our product candidates. If those collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.

In February 2015, we entered into a collaboration with Merck focused on the discovery, development and commercialization of biologics, including NGM313, NGM120, NGM217, NGM621, NGM395 and NGM386, but excluding aldafermin. In November 2018, Merck exercised its option to license NGM313. In March 2019, Merck exercised its option to extend the collaboration for an additional two years, from March 17, 2020 through March 16, 2022. The collaboration involves a complex allocation of rights, provides for substantial research and development support, provides for additional payments upon Merck's election to further extend the term of the research program and provides us with either milestone payments based on the achievement of specified clinical development, regulatory and commercial milestones and royalty-based revenue if certain product candidates are successfully commercialized or a cost and profit sharing arrangement with the possibility that we would provide sales representatives to co-detail the product candidates that Merck elects to advance in the United States. We cannot predict the success of the collaboration, including whether Merck exercises its option to license additional product candidates or terminates its license to a program. Merck's license to the GDF15 receptor agonist program, including NGM395 and NGM386, was terminated effective May 31, 2019.

We may seek other third-party collaborators for the development and commercialization of any product candidates that are not subject to the Merck collaboration, including aldafermin, NGM395 and NGM386. Our likely collaborators for any collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. If we enter into any such arrangements with any third parties, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenue from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

Collaborations involving our product candidates, including our collaboration with Merck, pose risks to us, including the following:

- Collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations. For example, under our collaboration with Merck, once proof-of-concept data in humans has been generated and Merck has exercised its option to acquire an exclusive license for a product candidate, our ability to influence the resources Merck devotes to such product candidate will be substantially reduced until such time, if any, that we exercise our right to participate in a cost and profit sharing arrangement. Even after we exercise that right to participate in a cost and profit sharing arrangement, our ability to influence Merck will be limited.

- Collaborators might opt not to pursue development and commercialization of our product candidates or not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding or external factors, such as an

acquisition that diverts resources or creates competing priorities. For example, Merck might opt not to exercise its option to acquire a license to a product candidate that has generated proof-of-concept data, or Merck may opt to terminate its license to a program, as it did for NGM395 and NGM386.

- Collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing. For example, under our agreement with Merck, it is possible for Merck to terminate the NGM313 program and any other program (whether or not we have exercised our cost and profit sharing option) upon prior written notice, without triggering a termination of the remainder of the collaboration arrangement.

- Collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our medicines or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours.

- A collaborator with marketing and distribution rights to one or more medicines might not commit sufficient resources to the marketing and distribution of our product candidates.

- Collaborators might not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation. For example, Merck has the first right to maintain or defend our intellectual property rights under the Collaboration Agreement with respect to certain licensed programs and, although we may have the right to assume the maintenance and defense of our intellectual property rights if Merck does not, our ability to do so may be compromised by Merck's actions.

- Disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our medicines or product candidates or that result in costly litigation or arbitration that diverts management attention and resources.

- We may lose certain valuable rights under circumstances identified in our collaborations, including, in the case of our agreement with Merck, if we undergo a change in control.

- Collaborations might be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.

- Collaboration agreements might not lead to development or commercialization of product candidates in the most efficient manner, or at all. If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development or commercialization program under such collaboration could be delayed, diminished or terminated.

Under certain circumstances, Merck may unilaterally terminate its annual funding of our research and development program, or terminate or shift the focus of its research and development funding, any of which would materially and adversely affect our business.

Under the Collaboration Agreement, Merck has the right to terminate all or part of the agreement at certain times and under certain circumstances. Merck may terminate the research and early development program effective March 17, 2022 by providing notice to us prior to March 17, 2021. Merck may terminate its annual funding of the research program prior to March 17, 2022 if we are acquired by a third party or if we are in material uncured breach of our obligations under the research and early development program. After the current term of the collaboration or, if Merck again exercises its option to extend the term, after such extension period, Merck may terminate the overall agreement for convenience upon written notice and subject to certain limitations.

Subject to certain limitations, Merck may partially terminate the Collaboration Agreement for convenience as it relates to NGM313 or any future Optioned Program. For example, Merck terminated its license to our GDF15 receptor agonist program, including NGM395 and NGM386, effective May 31, 2019. Merck may also terminate the agreement as it relates to its rights to research and develop small molecule compounds. It may also terminate

the agreement with respect to a specific Optioned Program, such as NGM313, in the event of an uncured material breach by us. If Merck terminates a program as a result of our uncured material breach, then we would lose our option to participate in global cost and profit sharing if not yet exercised as of the time of termination, and lose our co-detailing option (whether or not exercised as of that time) for the relevant Optioned Program.

If Merck terminates funding, terminates the Collaboration Agreement, decides not to further extend the research phase of the collaboration or shifts the focus of its research and development funding, it could impede our ability to fund and complete our research and development programs, which would materially and adversely affect our business.

We may not be able to obtain and maintain the third-party relationships that are necessary to develop, commercialize and manufacture some or all of our product candidates.

In addition to our dependence on our collaboration with Merck, we expect to depend on other collaborators, partners, licensees, CROs, clinical investigators, manufacturers and other third parties to support our discovery efforts, to formulate product candidates, to conduct clinical trials for some or all of our product candidates, to manufacture clinical and commercial scale quantities of our drug substances and drug products and to market, sell and distribute any products we successfully develop and for which we obtain regulatory approval. Any problems we experience with any of these third parties could delay our research efforts or the development, commercialization and manufacturing of our products or product candidates, which could harm our results of operations.

Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured product candidates or products ourselves, including reliance on third parties for regulatory compliance and quality assurance, the possibility of breach of the manufacturing agreement by third parties because of factors beyond our control (including a failure to manufacture our product candidates or any products we may eventually commercialize in accordance with our specifications) and the possibility of termination or nonrenewal of agreements by third parties, based on its own business priorities, at a time that is costly or damaging to us.

If any of our product candidates are approved by the FDA or other regulatory agencies for commercial sale, we or our collaborator may need to manufacture it in larger quantities. We intend to use third-party manufacturers for commercial quantities of aldafermin, NGM120, NGM217, NGM621 and NGM395, to the extent we advance these product candidates, and will rely on Merck to determine whether to utilize a third-party manufacturer or internal manufacturing capacity for NGM313 and other optioned product candidates. Our or our collaborator's manufacturers may not be able to successfully increase the manufacturing capacity for any of our product candidates in a timely or efficient manner, or at all. If we or our collaborator are unable to successfully increase the manufacturing capacity for a product candidate, the regulatory approval or commercial launch of that product candidate may be delayed or there may be a shortage in the supply of the product candidate. Our or our collaborator's failure or the failure of third-party manufacturers to comply with the FDA's cGMP and to pass inspections of the manufacturing facilities by the FDA or other regulatory agencies could seriously harm our business.

We cannot guarantee that we or, as applicable, our collaborator will be able to successfully negotiate agreements for, or maintain relationships with, collaborators, partners, licensees, CROs, clinical investigators, manufacturers and other third parties on favorable terms, if at all. If we or our collaborator are unable to obtain or maintain these agreements, we may not be able to clinically develop, formulate, manufacture, obtain regulatory approvals for or commercialize our product candidates, which will, in turn, adversely affect our business.

We and our collaborator expect to expend substantial management time and effort to enter into relationships with third parties and, if we or our collaborator successfully enter into such relationships, to manage these relationships. In addition, substantial capital will be paid to third parties in these relationships. However, we cannot control the amount or timing of resources our contract partners will devote to our research and development programs, product candidates or potential product candidates, and we cannot guarantee that these parties will fulfill their obligations to us under these arrangements in a timely fashion, if at all. In addition, we are less knowledgeable about the reputation and quality of third-party contractors in countries outside of the United States where we conduct discovery research or preclinical and clinical development and manufacturing of our product candidates and, therefore, enter into these relationships with less information than if these third parties were in the United States, we may not choose the best parties for these relationships.

We may seek to establish additional collaborations, and, if we are not able to establish them on commercially reasonable terms, we may have to alter our development and commercialization plans.

Our drug development programs and the potential commercialization of our product candidates will require substantial additional cash to fund expenses. For product candidates not partnered with Merck, such as aldafermin, NGM395 and NGM386, we may decide to collaborate with other pharmaceutical and biotechnology companies for their development and potential commercialization.

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 product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products and the existence of uncertainty with respect to our ownership of intellectual property, 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. Potential collaborators may also consider alternative product candidates or intellectual property for similar indications that may be available for collaboration and whether such an alternative collaboration could be more attractive than the one with us for our product candidate.

We may also be restricted under existing collaboration agreements from entering into future agreements on certain terms with potential collaborators. For example, under our Collaboration Agreement with Merck, we may not directly or indirectly research, develop, manufacture or commercialize, except pursuant to the agreement, any medicine or product candidate that modulates a target then subject to the collaboration with specified activity. The FGF19 program, including aldafermin, is excluded from this provision, notwithstanding that both aldafermin and NGM313 signal, in part, through the FGFR1c pathway. During the tail period following the research term, we may not directly or indirectly research, develop or commercialize, outside of the collaboration, any medicine or product candidate with specified activity against any collaboration target that has been designated a tail target.

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

We may not be able to negotiate 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 product 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 product candidates or bring them to market and generate product revenue.

We rely on third parties to conduct our clinical trials and some aspects of our research and preclinical testing, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research or testing.

We currently rely on, and expect to continue to rely on, third parties, such as CROs, clinical data management organizations, medical institutions, consultants and clinical investigators, to conduct our clinical trials and certain aspects of our research and preclinical testing. Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it would delay our product development activities and such alternative arrangements may not be available on terms acceptable to us.

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 responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with standards, commonly referred to as cGCP, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored

database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our medicines.

We also expect to rely on third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our medicines, producing additional losses and depriving us of potential product revenue.

In addition, we rely on these third parties to provide accurate financial information related to our research and development activities and if any inaccurate financial information were provided by these third parties, our results of operations could be adversely impacted.

We contract with third parties for the manufacture of our product candidates for preclinical testing and expect to continue to do so for clinical trials and for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our product candidates 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 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 commercial supply of any of these product candidates for which we or our collaborator obtains marketing approval. To date, we have obtained materials for aldafermin, NGM313, NGM120, NGM217, NGM621 and NGM395 for preclinical and clinical testing from third-party manufacturers. Other than for a long-term supply agreement with Lonza for aldafermin, we do not have a long-term supply agreement with any third-party manufacturer.

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

- 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
- reliance on the third party for regulatory compliance, quality assurance and safety and pharmacovigilance reporting.

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 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 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 medicines that we may develop may compete with other product candidates and products 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 redundant supply for 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 would 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 any future products may adversely affect our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis.

Risks Related to Regulatory Approvals

None of our product candidates has received regulatory approvals. If we are unable to obtain regulatory approvals to market one or more of our product candidates, our business will be adversely affected.

We do not expect our product candidates to be commercially available for several years, if at all. Our product candidates are subject to strict regulation by regulatory authorities in the United States and in other countries. We cannot market any product candidate until we have completed all necessary preclinical studies and clinical trials and have obtained the necessary regulatory approvals. We do not know whether regulatory agencies will grant approval for any of our product candidates. Even if we complete preclinical studies and clinical trials successfully, we may not be able to obtain regulatory approvals or we may not receive approvals to make claims about our products that we believe to be necessary to effectively market our products. Data obtained from preclinical studies and clinical trials is subject to varying interpretations that could delay, limit or prevent regulatory approval, and failure to comply with regulatory requirements or inadequate manufacturing processes are examples of other problems that could prevent approval. In addition, we may encounter delays or rejections due to additional government regulation from future legislation, administrative action or changes in the policies of the FDA or comparable foreign regulatory authorities. Even if the FDA or a comparable foreign regulatory authority approves a product, the approval will be limited to those indications covered in the approval.

The regulatory approval processes of the FDA and comparable foreign regulatory authorities are lengthy, time-consuming and inherently unpredictable. Our inability to obtain regulatory approval for our product candidates would substantially harm our business.

Currently, none of our product candidates has received regulatory approval. The time required to obtain approval from the FDA and comparable foreign regulatory authorities is unpredictable but typically takes many years following the commencement of preclinical studies and 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 preclinical and clinical data necessary to gain approval may change during the course of a product candidate's development and may vary among jurisdictions. It is possible that none of our existing or future product candidates will ever obtain regulatory approval.

Our product candidates could fail to receive regulatory approval from the FDA or a comparable foreign regulatory authority for many reasons, including:

- disagreement with the design or implementation of our clinical trials;
- failure to demonstrate that a product candidate is safe and effective for its proposed indication;
- failure of results of clinical trials to meet the level of statistical significance required for approval;
- failure to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- disagreement with our interpretation of data from preclinical studies or clinical trials;
- the insufficiency of data collected from clinical trials of our product candidates to support the submission and filing of a BLA or other submission or to obtain regulatory approval;
- failure to obtain approval of the manufacturing processes or facilities of third-party manufacturers with whom we contract for clinical and commercial supplies; or

- changes in the approval policies or regulations that render our preclinical and clinical data insufficient for approval.

The FDA or a comparable foreign regulatory authority may require more information, including additional preclinical or clinical data, to support approval, which may delay or prevent approval and our commercialization plans, or we may decide to abandon the development program for other reasons. 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 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.

We have received orphan drug status for aldafermin for PBC in the United States and for PBC and PSC in the EU. The FDA grants orphan drug designation to drugs intended to treat a rare disease or condition, which is generally defined as a disease or condition that affects fewer than 200,000 individuals in the United States and fewer than five in 10,000 individuals in the EU. Typically, 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 or the EMA, from approving another marketing application for the same drug for that time period. The applicable period is seven years in the United States and 10 years in the EU. The EU exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or EMA 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.

Although we have obtained orphan drug status for aldafermin for PBC and PSC, that exclusivity may not effectively protect the candidate 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. Any inability to secure orphan drug designation or the exclusivity benefits of this designation could have an adverse impact on our ability to develop and commercialize our product candidates. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. Obtaining orphan drug designation may not provide us with a material commercial advantage.

The FDA has a Fast Track program that is intended to expedite or facilitate the process for reviewing new drug products that meet certain criteria. Specifically, new drugs are eligible for Fast Track designation if they 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. Unique to a Fast Track product, the FDA may consider sections of the BLA for review on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the BLA, the FDA agrees to accept sections of the BLA and determines that the schedule is acceptable and the sponsor pays any required user fees upon submission of the first section of the BLA. Fast Track designation does not change the standards for product approval.

Although aldafermin has received Fast Track designation from the FDA for PBC and NASH, we may not necessarily experience faster development timelines or achieve faster review or approval compared to conventional FDA procedures. Access to an expedited program may also be withdrawn by the FDA if it believes that the designation is no longer supported by data from our clinical development program. Additionally, qualification for any expedited review procedure does not ensure that we will ultimately obtain regulatory approval for aldafermin or any other product candidate that we are developing or may develop.

Our failure to obtain regulatory approval in international jurisdictions would prevent us from marketing our product candidates outside the United States.

If we or our collaborators succeed in developing any products, we intend to market them in the EU and other foreign jurisdictions in addition to the United States. In order to market and sell our products in other jurisdictions, we 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, we must secure product reimbursement approvals before regulatory authorities will approve the product for sale in that country. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. Further, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries and regulatory approval in one country does not ensure approval in any other country, while a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory approval process in others. Also, regulatory approval for any of our product candidates may be withdrawn if we fail to comply with regulatory requirements, if problems occur after the product candidate reaches the market or for other reasons. If we fail to comply with the regulatory requirements in international markets and fail to receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed and our business will be adversely affected. We may not obtain foreign regulatory approvals on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions. 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. If we fail to obtain approval of any of our product candidates by regulatory authorities in another country, we will be unable to commercialize our product in that country, and the commercial prospects of that product candidate and our business prospects could decline.

Even if our product candidates receive regulatory approval, they may still face future development and regulatory difficulties.

Even if we obtained regulatory approval for a product candidate, it would be subject to ongoing requirements by the FDA and comparable foreign regulatory authorities governing the manufacture, quality control, further development, labeling, packaging, storage, distribution, safety surveillance, import, export, advertising, promotion, recordkeeping and reporting of safety and other post-market information. The FDA and comparable foreign regulatory authorities will continue to closely monitor the safety profile of any product even after approval. If the FDA or comparable foreign regulatory authorities become aware of new safety information after approval of any of our product candidates, they may require labeling changes or establishment of a REMS or similar strategy, impose significant restrictions on a product's indicated uses or marketing or impose ongoing requirements for potentially costly post-approval studies or post-market surveillance.

In addition, manufacturers of drug products and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP regulations and standards. If we or a regulatory agency discover previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions on that product, the manufacturing facility or us, including requiring recall or withdrawal of the product from the market or suspension of manufacturing. If we, our product candidates or the manufacturing facilities for our product candidates fail to comply with applicable regulatory requirements, or undesirable side effects caused by such products are identified, a regulatory agency may:

- issue safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings about such product;
- mandate modifications to promotional materials or require us to provide corrective information to healthcare practitioners;
- require that we conduct post-marketing studies;

- require us to enter into a consent decree, which can include imposition of various fines, reimbursements for inspection costs, required due dates for specific actions and penalties for noncompliance;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend marketing of, withdraw regulatory approval of or recall such product;
- suspend any ongoing clinical trials;
- refuse to approve pending applications or supplements to applications filed by us;
- suspend or impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products, refuse to permit the import or export of products or require us to initiate a product recall.

The occurrence of any event or penalty described above may inhibit our ability to commercialize our products and generate revenue.

Advertising and promotion of any product candidate that obtains approval in the United States will be heavily scrutinized by the FDA, DOJ, HHS' Office of Inspector General, state attorneys general, members of Congress and the public. Violations, including promotion of our products for unapproved (or off-label) uses, are subject to enforcement letters, inquiries and investigations and civil and criminal sanctions by the government. Additionally, comparable foreign regulatory authorities will heavily scrutinize advertising and promotion of any product candidate that obtains approval outside of the United States.

In the United States, engaging in the impermissible promotion of our products for off-label uses can also subject us to false claims litigation under federal and state statutes, which can lead to civil and criminal penalties and fines and agreements that materially restrict the manner in which a company promotes or distributes drug products. These false claims statutes include the federal FCA, which allows any individual to bring a lawsuit against a pharmaceutical company on behalf of the federal government alleging submission of false or fraudulent claims, or causing to present such false or fraudulent claims, for payment by a federal program such as Medicare or Medicaid. If the government prevails in the lawsuit, the individual will share in any fines or settlement funds. Since 2004, these FCA lawsuits against pharmaceutical companies have increased significantly in volume and breadth, leading to several substantial civil and criminal settlements regarding certain sales practices promoting off-label drug uses involving fines in excess of $1 billion. This growth in litigation has increased the risk that a pharmaceutical company will have to defend a false claim action, pay settlement fines or restitution, agree to comply with burdensome reporting and compliance obligations and be excluded from Medicare, Medicaid and other federal and state healthcare programs. If we do not lawfully promote our approved products, we may become subject to such litigation and, if we do not successfully defend against such actions, those actions may have a material adverse effect on our business, financial condition and results of operations.

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.

Even if we are able to obtain regulatory approvals for any of our product candidates, if they exhibit harmful side effects after approval, our regulatory approvals could be revoked or otherwise negatively impacted, and we could be subject to costly and damaging product liability claims.

Even if we receive regulatory approval for aldafermin or any of our other product candidates, we will have tested them in only a small number of patients during our clinical trials. If our applications for marketing are approved and more patients begin to use our product, new risks and side effects associated with our products may be discovered. As a result, regulatory authorities may revoke their approvals. If aldafermin is approved by the FDA based on a surrogate endpoint pursuant to accelerated approval regulations (Subpart E regulations), we will be required to conduct additional clinical trials establishing clinical benefit on the ultimate outcome of NASH. Additionally, we may be required to conduct additional clinical trials, make changes in labeling of our product, reformulate our product or make changes and obtain new approvals for our and our suppliers' manufacturing facilities for aldafermin and our other product candidates. We might have to withdraw or recall our products from the marketplace. We may also experience a significant drop in the potential sales of our product if and when regulatory approvals for such product are obtained, experience harm to our reputation in the marketplace or become subject to lawsuits, including class actions. Any of these results could decrease or prevent any sales of our approved product or substantially increase the costs and expenses of commercializing and marketing our product.

Risks Related to Our Intellectual Property

Our success depends upon our ability to obtain and maintain intellectual property protection for our products and technologies.

Our success will depend in significant part on our and our current or future licensors', licensees' or collaborators' ability to establish and maintain adequate protection of our intellectual property covering the product candidates we plan to develop, and the ability to develop these product candidates and commercialize the products resulting therefrom, without infringing the intellectual property rights of others. In addition to taking other steps to protect our intellectual property, we have applied for, and intend to continue to apply for, patents with claims covering our technologies, processes and product candidates when and where we deem it appropriate to do so. We have filed numerous patent applications both in the United States and in certain foreign jurisdictions to obtain patent rights to inventions we have discovered, with claims directed to compositions of matter, methods of use, formulations, combination therapy and other technologies relating to our product candidates. There can be no assurance that any of these patent applications will issue as patents or, for those applications that do mature into patents, whether the claims of the patents will exclude others from making, using or selling our product candidates or products that are substantially similar to our product candidates. In countries where we have not and do not seek patent protection, third parties may be able to manufacture and sell our product candidates without our permission, and we may not be able to stop them from doing so.

Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing or, in some cases, not at all until they are issued as a patent. Therefore, we cannot be certain that we or our current or future licensors, licensees or collaborators were the first to make the inventions claimed in our owned or licensed patents or pending patent applications, or that we or our current or future licensors, licensees or collaborators were the first to file for patent protection of such inventions.

Any changes we make to our product candidates, including aldafermin, NGM313, NGM120, NGM217, NGM621 and NGM395, to cause them to have what we view as more advantageous properties may not be covered by our existing patents and patent applications, and we may be required to file new patent applications and/or seek other forms of protection for any such altered product candidates. The patent landscape surrounding the technology underlying our product candidates is crowded, and there can be no assurance that we would be able to secure patent protection that would adequately cover an alternative to our aldafermin molecule, including half-life extending formulation enhancements or the half-life extended variants of FGF19 that we are developing, NGM313, NGM120, NGM217, NGM621 and NGM395 or any of our other product candidates.

We do not currently own or have a license to any issued patents that cover our NGM217 or NGM621 product candidates, although they are disclosed and claimed in our pending U.S. non-provisional and/or PCT applications and/or national stage applications in particular foreign countries. The patent landscape surrounding NGM217 and NGM621 is crowded, and there can be no assurance that we will be able to secure patent protection that would adequately cover such product candidates, nor can there be any assurance that we would obtain sufficiently broad claims to be able to prevent others from selling competing products.

The patent prosecution process is expensive and time-consuming, and we and our current or future licensors, licensees or collaborators may not be able to prepare, file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we or our current or future licensors, licensees or collaborators will fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection for them. Moreover, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain or enforce the patents, covering technology that we license from or license to third parties and may be reliant on our current or future licensors, licensees or collaborators to perform these activities, which means that these patent applications may not be prosecuted, and these patents may not be enforced, in a manner consistent with the best interests of our business. If our current or future licensors, licensees or collaborators fail to establish, maintain, protect or enforce such patents and other intellectual property rights, such rights may be reduced or eliminated. If our current or future licensors, licensees or collaborators are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised.

Similar to other biotechnology companies, our patent position is generally highly uncertain and involves complex legal and factual questions. The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our patents may be challenged in the courts or patent offices in the United States and abroad. In recent years, these areas have been the subject of much litigation in the industry. As a result, the issuance, scope, validity, enforceability and commercial value of our and our current or future licensors', licensees' or collaborators' patent rights are highly uncertain. Our and our current or future licensors', licensees' or collaborators' pending and future patent applications may not result in patents being issued that protect our technology or product candidates, or products resulting therefrom, in whole or in part, or that effectively prevent others from commercializing competitive technologies and products. The patent examination process may require us or our current or future licensors, licensees or collaborators to narrow the scope of the claims of pending and future patent applications, which would limit the scope of patent protection that is obtained, if any. Our and our current or future licensors', licensees' or collaborators' patent applications cannot be enforced against third parties practicing the technology that is currently claimed in such applications unless and until a patent issues from such applications, and then only to the extent the claims that issue are broad enough to cover the technology being practiced by third parties.

Furthermore, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after the resulting products are commercialized. As a result, our owned and in-licensed patents may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours and we may need to rely solely on regulatory or similar protections, if they are available. We expect to seek extensions of patent terms for our issued patents, where available. In the United States, this includes under the Hatch-Waxman Act, which permits a patent term extension of up to five years beyond the original expiration date of the patent as compensation for regulatory delays. However, such a patent term extension cannot lengthen the remaining term of a patent beyond a total of 14 years from the product's approval date. Only one patent applicable to an approved drug is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. During the period of patent term extension, the claims of a patent are not enforceable for their full scope, but are instead limited to the scope of the approved product. In addition, the applicable authorities, including the FDA in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. In addition, we may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to the expiration of relevant patents or otherwise failing to satisfy applicable requirements. If this occurs, any period during which we have the right to exclusively market our product will be shorter than we would otherwise expect, and our competitors may obtain approval of and launch products earlier than might otherwise be the case.

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

The legal protection afforded to inventors and owners of intellectual property in countries outside of the United States may not be as broad or effective as that in the United States and we may, therefore, be unable to acquire and enforce intellectual property rights outside the United States to the same extent as in the United States. Whether filed in the United States or abroad, our patent applications may be challenged or may fail to result in issued patents.

In addition, our existing patents and any future patents we obtain may not be sufficiently broad to prevent others from practicing our technologies or from developing or commercializing competing products. Furthermore, others may independently develop or commercialize similar or alternative technologies or drugs, or design around our patents. Our patents may be challenged, invalidated, circumvented or narrowed, or fail to provide us with any competitive advantages. In many foreign countries, patent applications and/or issued patents, or parts thereof, must be translated into the native language. If our patent applications or issued patents are translated incorrectly, they may not adequately cover our technologies; in some countries, it may not be possible to rectify an incorrect translation, which may result in patent protection that does not adequately cover our technologies in those countries.

Filing, prosecuting, enforcing and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States are 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 certain state laws in the United States. Consequently, we and our collaborator may not be able to prevent third parties from practicing our and our collaborator's inventions in all countries outside the United States, or from selling or importing products made using our and our collaborator's inventions in and into the United States or other jurisdictions. Competitors may use our and our collaborator's technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we and our collaborator have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our product candidates and our and our collaborator's 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 and other intellectual property protection, particularly those relating to biopharmaceuticals. This could make it difficult for us and our collaborator to stop the infringement of our and our collaborator's patents or the marketing of competing products in violation of our and our collaborator's proprietary rights, generally. Proceedings to enforce our and our collaborator's patent rights in foreign jurisdictions could result in substantial costs and divert our and our collaborator's efforts and attention from other aspects of our business, could put our and our collaborator's patents at risk of being invalidated or interpreted narrowly, could place our and our collaborator's patent applications at risk of not issuing and could provoke third parties to assert claims against us or our collaborator. We or our collaborator may not prevail in any lawsuits that we or our collaborator initiate and the damages or other remedies awarded, if any, may not be commercially meaningful.

The requirements for patentability differ in certain countries, particularly developing countries. For example, China has a heightened requirement for patentability and, specifically, requires a detailed description of medical uses of a claimed drug. In addition, India, certain countries in Europe and certain developing countries, including Thailand, have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In those countries, we and our collaborator may have limited remedies if patents are infringed or if we or our collaborator are compelled to grant a license to a third party, which could materially diminish the value of those patents. This could limit our potential revenue opportunities. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. Accordingly, our and our collaborator's efforts to enforce intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we own or license.

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

Periodic maintenance and annuity fees on issued United States patents and most foreign patent applications and patents must be paid to the USPTO, and foreign patent agencies, respectively, in order to maintain such patents and patent applications. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application, examination and issuance processes. While an inadvertent lapse can be cured, in some cases, by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we or our collaborator fail to maintain the patents and patent applications covering our product candidates, our competitors might be able to enter the market with similar or identical products or technologies, which would have a material adverse effect on our business, financial condition and results of operations.

Changes in patent law could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.

As is the case with other biotechnology and pharmaceutical companies, our success is heavily dependent on intellectual property rights, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involves technological and legal complexity, and obtaining and enforcing biopharmaceutical patents is costly, time-consuming and inherently uncertain. The U.S. Supreme Court and the United States Court of Appeals for the Federal Circuit have ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances, weakening the rights of patent owners in certain situations or ruling that certain subject matter is not eligible for patent protection. In addition to increasing uncertainty with regard to our and our collaborator's ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents once obtained. Depending on decisions by Congress, the federal courts, the USPTO and equivalent bodies in foreign jurisdictions, the laws and regulations governing patents could change in unpredictable ways that would weaken our and our collaborator's ability to obtain new patents or to enforce existing patents and patents we and our collaborator may obtain in the future.

Patent reform laws, such as the Leahy-Smith America Invents Act (the "Leahy-Smith Act"), and changes in how patent laws are interpreted could increase the uncertainties and costs surrounding the prosecution of our and our collaborator's patent applications and the enforcement or defense of our or our collaborator's issued patents. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the filing and prosecution strategies associated with patent applications, including a change from a "first-to-invent" to a "first-inventor-to-file" patent system. Other provisions also may affect patent prosecution and litigation, such as by allowing third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent by USPTO-administered post-grant proceedings, including post-grant review, *inter partes* review and derivation proceedings. The USPTO has developed regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act and, in particular, the "first-inventor-to-file" provisions, became effective in 2013. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our or our collaborator's patent applications and the enforcement or defense of our or our collaborator's issued patents, all of which could have a material adverse effect on our business, financial condition and results of operations.

We may be unable to obtain intellectual property rights or technologies necessary to develop and commercialize our product candidates.

Several third parties are actively researching and seeking and obtaining patent protection in the cardio-metabolic disease, NASH, liver disease, oncology and ophthalmic fields, and there are issued third-party patents and published third-party patent applications in these fields. The patent landscape around our aldafermin, NGM313, NGM120, NGM217, NGM621 and NGM395 product candidates is complex, and we are aware of several third-party patents and patent applications containing claims directed to compositions of matter, methods of use and related subject matter, some of which pertain, at least in part, to subject matter that might be relevant to our aldafermin, NGM313, NGM120, NGM217, NGM621 and NGM395 product candidates. However, we may not be aware of all third-party intellectual property rights potentially relating to our product candidates and technologies.

Depending on what patent claims ultimately issue and how courts construe the issued patent claims, as well as depending on the ultimate formulation and method of use of our product candidates, we may need to obtain a license to practice the technology claimed in such patents. There can be no assurance that such licenses will be available on commercially reasonable terms, or at all. If a third party does not offer us a necessary license or offers a license only on terms that are unattractive or unacceptable to us, we might be unable to develop and commercialize one or more of our product candidates, which would have a material adverse effect on our business, financial condition and results of operations. Moreover, even if we obtain licenses to such intellectual property, but subsequently fail to meet our obligations under our license agreements, or such license agreements are terminated for any other reason, we may lose our rights to in-licensed technologies.

The licensing or acquisition of third-party intellectual property rights is a competitive area, and more established companies may pursue strategies to license or acquire third-party intellectual property rights that we may consider attractive or necessary. These established companies may have a competitive advantage over us due to their size, capital resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment, or at all. If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of the relevant program or product candidate, which could have a material adverse effect on our business, financial condition, results of operations and prospects.

We may become involved in lawsuits or other proceedings to protect or enforce our intellectual property, which could be expensive, time-consuming and unsuccessful and have a material adverse effect on the success of our business.

Third parties may infringe our or our collaborator's patents or misappropriate or otherwise violate our or our collaborator's intellectual property rights. In the future, we or our collaborator may initiate legal proceedings to enforce or defend our or our collaborator's intellectual property rights, to protect our or our collaborator's trade secrets or to determine the validity or scope of intellectual property rights we own or control. Also, third parties may initiate legal proceedings against us or our collaborator to challenge the validity or scope of intellectual property rights we own, control or to which we have rights. For example, generic or biosimilar drug manufacturers or other competitors or third parties may challenge the scope, validity or enforceability of our or our collaborator's patents, requiring us or our collaborator to engage in complex, lengthy and costly litigation or other proceedings. These proceedings can be expensive and time-consuming and many of our or our collaborator's adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we or our collaborator can. Accordingly, despite our or our collaborator's efforts, we or our collaborator may not be able to prevent third parties from infringing upon or misappropriating intellectual property rights we own, control or have rights to, particularly in countries where the laws may not protect those rights as fully as in the United States. Litigation could result in substantial costs and diversion of management resources, which could harm our business and financial results. In addition, if we or our collaborator initiated legal proceedings against a third party to enforce a patent covering a product candidate, the defendant could counterclaim that such patent is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during

prosecution. In an infringement or declaratory judgment proceeding, a court may decide that a patent owned by or licensed to us is invalid or unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our or our collaborator's patents do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our or our collaborator's patents at risk of being invalidated, narrowed, held unenforceable or interpreted in such a manner that would not preclude third parties from entering the market with competing products.

Third-party pre-issuance submission of prior art to the USPTO, opposition, derivation, revocation, reexamination, *inter partes* review or interference proceedings, or other pre-issuance or post-grant proceedings, as well as other patent office proceedings or litigation in the United States or other jurisdictions provoked by third parties or brought by us or our collaborator, may be necessary to determine the inventorship, priority, patentability or validity of inventions with respect to our or our collaborator's patents or patent applications. An unfavorable outcome could leave our technology or product candidates without patent protection, allow third parties to commercialize our technology or product candidates and compete directly with us, without payment to us, or could require us or our collaborator to obtain license rights from the prevailing party in order to be able to manufacture or commercialize our product candidates without infringing third-party patent rights. Our business could be harmed if the prevailing party does not offer us or our collaborator a license on commercially reasonable terms, or at all. Even if we or our collaborator obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us or our collaborator. In addition, if the breadth or strength of protection provided by our or our collaborator's patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates. Even if we successfully defend such litigation or proceeding, we may incur substantial costs and it may distract our management and other employees.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, many foreign jurisdictions have rules of discovery that are different than those in the United States and that may make defending or enforcing our or our collaborator's patents extremely difficult. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of shares of our common stock.

Third parties may initiate legal proceedings against us alleging that we infringe their intellectual property rights or we may initiate legal proceedings against third parties to challenge the validity or scope of intellectual property rights controlled by third parties, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability and the ability of our collaborator to develop, manufacture, market and sell any product candidates that we may develop and use our proprietary technologies without infringing, misappropriating or otherwise violating the intellectual property and proprietary rights of third parties. The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights. Third parties may initiate legal proceedings against us or our collaborator alleging that we or our collaborator infringe their intellectual property rights or we or our collaborator may initiate legal proceedings against third parties to challenge the validity or scope of intellectual property rights controlled by third parties, including in oppositions, interferences, revocations, reexaminations, *inter partes* review or derivation proceedings before the USPTO or its counterparts in other jurisdictions. These proceedings can be expensive and time-consuming and many of our or our collaborator's adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we or our collaborator can.

For example, through our European representative, we filed an opposition in the EPO, to a patent granted to St. Vincent's Hospital Sydney Limited ("St. Vincent's") claiming the use of MIC-1, also known as GDF15, in the treatment of obesity. In the first instance proceedings, the Opposition Division at the EPO upheld the patent as granted. We have appealed this decision to the Board of Appeals at the EPO and oral proceedings in that appeal are scheduled for August 2020. The St. Vincent's patent as granted is currently scheduled to expire in April 2025. Should the patent be upheld on appeal or should we decide not to pursue the appeal, we do not believe that NGM395 would be able to be commercially launched until after expiration of the patent.

We filed an opposition in the EPO to a patent granted to Amgen claiming the use of GDF15 polypeptides for the treatment of several metabolic disorders. At the first instance proceedings, the Opposition Division at the EPO maintained the patent in amended form, with claims not including obesity, an indication for which we may pursue a regulatory approval for NGM395. We appealed the decision to maintain the patent to the Board of Appeals at the EPO in September 2019. The Amgen patent as granted is currently scheduled to expire in April 2032. If these patents have not expired, or are not ultimately deemed invalid in appeals stemming from the opposition proceedings, and/or our non-infringement positions are not upheld, and these patents are successfully asserted against us in a European country court proceeding after any future potential approval of our NGM395 product candidate for the treatment of obesity in Europe, then we may be required to obtain licenses to such patents in order to commercialize NGM395, and there can be no assurance that such licenses would be available on commercially reasonable terms, or at all.

In November 2018, we filed an opposition in the EPO to a patent granted to Genentech claiming the use of an anti-KLB agonistic antibody for treating diabetes mellitus or insulin resistance. We are one of two opponents challenging the Genentech patent as granted on numerous grounds, including lack of novelty and inventive step, insufficiency and claiming subject matter that extends beyond the application as originally filed. Genentech filed its response to opposition in April 2019, and the Company filed a response to the Genentech submission in June 2019 and oral proceedings were held in February 2020. The Genentech patent is currently scheduled to expire in April 2028. If the Genentech patent is not invalidated in the opposition proceedings and appeals, has not expired and/or our non-infringement positions are not upheld, and this patent is successfully asserted against us or our collaborator in a European country court proceeding after any future potential approval of our NGM313 product candidate for the treatment of diabetes and/or NASH in Europe, then we and/or our collaborator may be required to obtain a license to this patent in order to commercialize our NGM313 product candidate, and there can be no assurance that such license would be available on commercially reasonable terms, or at all.

An unfavorable outcome in any such proceeding could require us or our collaborator to cease using the related technology or developing or commercializing our product candidates, or to attempt to license rights to it from the prevailing party, which may not be available on commercially reasonable terms, or at all.

We could be found liable for monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could materially harm our business.

We perform searches of patent and scientific databases in order to identify documents that may be of potential relevance to the freedom-to-operate and/or patentability of our product candidates. In general, such searches are conducted based on keywords, sequences, inventors/authors and assignees/entities to capture U.S. and European patents and patent applications, PCT publications and scientific journal articles. There can be no assurance that such searches will identify all potentially relevant patents or patent applications, and the failure to identify any such patents or patent applications could have a material adverse effect on the commercialization of our product candidates.

We are aware of several third-party patents and patent applications containing claims directed to compositions of matter, methods of use and related subject matter, some of which pertain, at least in part, to subject matter that might be relevant to our aldafermin, NGM313, NGM120, NGM217, NGM621 and NGM395 product candidates. We are not aware of any facts that would lead us to conclude that the valid and enforceable claims of any third-party patents would reasonably be interpreted to encompass our product candidates, unless we are unsuccessful in our opposition of any of the granted European patents that are discussed above, or any appeals stemming therefrom. As to pending third-party applications, we cannot predict with any certainty which claims will issue, if any, or the scope of such issued claims. Even if we believe third-party intellectual property claims are without merit, there is no assurance that a court would find in our favor on questions of infringement, validity, enforceability or priority. A court of competent jurisdiction could hold that these third-party patents are valid, enforceable and infringed, which could materially and adversely affect our ability and the ability of our collaborator to commercialize any product candidates we may develop and any other product candidates or technologies covered by the asserted third-party patents. In order to successfully challenge the validity of any such U.S. patent in federal court, we would need to overcome a presumption of validity. As this burden is a high one requiring us to present clear and convincing evidence as to the invalidity of any such U.S. patent claim, there is no assurance that a court of competent jurisdiction would invalidate the claims of any such U.S. patent. If any such third-party patents (including those that may issue from such applications) were successfully asserted against us or our

collaborator or other commercialization partners and we were unable to successfully challenge the validity or enforceability of any such asserted patents, then we or our collaborator and other commercialization partners may be prevented from commercializing our product candidates, or may be required to pay significant damages, including treble damages and attorneys' fees if we are found to willfully infringe the asserted patents, or obtain a license to such patents, which may not be available on commercially reasonable terms, or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us, and it could require us to make substantial licensing and royalty payments. Any of the foregoing would have a material adverse effect on our business, financial condition and operating results.

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

Many of our employees, including our senior management, were previously employed at universities or at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Most of these employees executed proprietary rights, non-disclosure and non-competition agreements in connection with such previous employment. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed confidential information or intellectual property, including trade secrets or other proprietary information, of any such employee's former employer, or that third parties have an interest in our patents as an inventor or co-inventor. Litigation may be necessary to defend against these claims. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel or sustain other damages. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products. Such a license may not be available on commercially reasonable terms, or at all. Even if we successfully prosecute or defend against such claims, litigation could result in substantial costs and distract management.

In addition, while it is our policy to require our employees and contractors who may be involved in the conception or development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who, in fact, conceives or develops intellectual property that we regard as our own. The assignment of intellectual property rights may not be self-executing, or the assignment agreements may be breached, and we may be forced to bring claims against third parties, or defend claims that they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial condition, results of operations and prospects.

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

We or our licensors may be subject to claims that former employees, collaborators or other third parties have an interest in our owned or in-licensed patents, trade secrets, or other intellectual property as an inventor or co-inventor. For example, we or our licensors may have inventorship disputes arise from conflicting obligations of employees, 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 our or our licensors' ownership of our owned or in-licensed patents, trade secrets or other intellectual property. If we or our licensors fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property that is important to our product candidates. 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. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

If we breach any license agreement related to our product candidates, we could lose the ability to continue the development and commercialization of our product candidates.

Our commercial success depends upon our ability, and the ability of our licensors and collaborator, to develop, manufacture, market and sell our product candidates and use our and our collaborator's proprietary technologies without infringing the proprietary rights of third parties. A third party may hold intellectual property rights, including patent rights, that are important or necessary to the development of our products. As a result, we are a party to a number of technology licenses that are important to our business and expect to enter into additional licenses in the future. If we fail to comply with the obligations under these agreements, including payment and diligence obligations, our licensors may have the right to terminate these agreements, in which event we may not be able to develop, manufacture, market or sell any product that is covered by these agreements or to engage in any other activities necessary to our business that require the freedom-to-operate afforded by the agreements, or we may face other penalties under the agreements. For example, we are party to license agreements with multiple vendors under which we license cell lines used to produce multiple product candidates, including some that are currently subject to our collaboration with Merck. We require prior consent from some of these vendors to grant sub-licenses under these agreements. Therefore, these vendors may be able to prevent us from granting sub-licenses to third parties, which could affect our ability or Merck's ability to use certain desired manufacturers in order to manufacture our product candidates.

Any of the foregoing could materially adversely affect the value of the product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements may result in our having to negotiate new or amended agreements, which may not be available to us on equally favorable terms, or at all, or cause us to lose our rights under these agreements, including our rights to intellectual property or technology important to our development programs.

Our inability to protect our confidential information and trade secrets would harm our business and competitive position.

In addition to seeking patents for some of our technology and products, we also rely substantially on trade secrets in our activities, including unpatented know-how, technology and other proprietary materials and information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. However, these steps may be inadequate, we may fail to enter into agreements with all such parties or any of these parties may breach the agreements and disclose our proprietary information and there may be no adequate remedy available for such breach of an agreement. We cannot assure you that our proprietary information will not be disclosed or that we can meaningfully protect our trade secrets. 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 both within and outside the United States may be less willing, or unwilling, to protect trade secrets. If a competitor lawfully obtained or independently developed any of our trade secrets, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position.

Intellectual property rights do not necessarily address all potential threats.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make products that are similar to any product candidates we may develop or utilize similar technologies that are not covered by the claims of the patents that we license or may own in the future;
- we, or our current or future collaborators, might not have been the first to make the inventions covered by the issued patents and pending patent applications that we license or may own in the future;
- we, or our current or future collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our owned or licensed intellectual property rights;
- it is possible that our pending patent applications or those that we may own in the future will not lead to issued patents;
- issued patents to which we hold rights may be held invalid or unenforceable, including as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable;
- the patents of others may harm our business; and
- we may choose not to file a patent application in order to maintain certain trade secrets or know-how, and a third party may subsequently file a patent covering such intellectual property.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations and prospects.

Risks Related to Ownership of Our Common Stock

The market price of our stock has been and may continue to be volatile, and you could lose all or part of your investment.

The market price for our common stock has fluctuated significantly from time to time, for example, varying between a high of $20.50 on December 18, 2019 and a low of $8.81 on October 7, 2019. The trading price of our common stock has been and may continue to be highly volatile and subject to wide fluctuations in response to various factors, some of which we cannot control. In addition to the factors discussed in this *"Risk Factors"* section, these factors include:

- developments associated with our collaboration with Merck, including any non-renewal, termination or other change in our relationship with Merck;
- the success of competitive products or technologies;
- regulatory actions with respect to our product candidates or our competitors' product candidates or products;

- results of clinical trials of our product candidates or those of our competitors;
- actual or anticipated changes in our growth rate relative to our competitors;
- announcements by us or our competitors or collaborators of significant acquisitions, strategic collaborations, joint ventures, collaborations or capital commitments;
- regulatory, legal or payor developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- the results of our efforts to in-license or acquire additional product candidates or products;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- share price and volume fluctuations attributable to inconsistent trading volume levels of our shares;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or our other stockholders;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors; and
- general economic, industry and market conditions.

In addition, the stock market in general, and the Nasdaq Global Select Market and biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies, including very recently in connection with the ongoing COVID-19 pandemic, which has resulted in decreased stock prices for many companies notwithstanding the lack of a fundamental change in their underlying business models or prospects. Broad market and industry factors, including potentially worsening economic conditions and other adverse effects or developments relating to the ongoing COVID-19 pandemic, may negatively affect the market price of our common stock, regardless of our actual operating performance. The realization of any of the above risks or any of a broad range of other risks, including those described in this *"Risk Factors"* section, could have a dramatic and material adverse impact on the market price of our common stock.

Because of potential volatility in our trading price and trading volume, we may incur significant costs from class action securities litigation.

Holders of stock in companies that have a volatile stock price frequently bring securities class action litigation against the company that issued the stock. We may be the target of this type of litigation in the future. If any of our stockholders were to bring a lawsuit of this type against us, even if the lawsuit is without merit, we could incur substantial costs defending the lawsuit and the time and attention of our management could be diverted from other business concerns, either of which could seriously harm our business.

An active trading market for our common stock may not be sustained.

Our common stock is currently listed on the Nasdaq Global Select Market under the symbol “NGM” and trades on that market. We cannot assure you that an active trading market for our common stock will be sustained. Accordingly, we cannot assure you of the liquidity of any trading market, your ability to sell your shares of our common stock when desired, or the prices that you may obtain for your shares.

Our principal stockholders, including entities affiliated with The Column Group, Merck and management, own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

Our executive officers, directors, significant stockholders, including The Column Group and Merck, and their respective affiliates beneficially own a significant amount of our voting stock. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders 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. The interests of this group of stockholders may not always coincide with your interests or the interests of other stockholders. In addition, if any of our significant stockholders decide to sell a meaningful amount of their ownership position and there is not sufficient demand in the market for such stocks, our stock price could fall.

We are an “emerging growth company” as defined in the JOBS Act and will be able to avail ourselves of reduced disclosure requirements applicable to emerging growth companies, which could make our common stock less attractive to investors and adversely affect the market price of our common stock.

For so long as we remain an “emerging growth company” as defined in the JOBS Act, we may take advantage of certain exemptions from various requirements applicable to public companies that are not “emerging growth companies” including:

- the provisions of Section 404(b) of the Sarbanes-Oxley Act of 2002 (the “Sarbanes-Oxley Act”) requiring that our independent registered public accounting firm provide an attestation report on the effectiveness of our internal control over financial reporting;

- the “say on pay” provisions (requiring a non-binding stockholder vote to approve compensation of certain executive officers) and the “say on golden parachute” provisions (requiring a non-binding stockholder vote to approve golden parachute arrangements for certain executive officers in connection with mergers and certain other business combinations) of the Dodd-Frank Wall Street Reform and Protection Act (the “Dodd-Frank Act”) and some of the disclosure requirements of the Dodd-Frank Act relating to compensation of our chief executive officer; and

- the requirement to provide detailed compensation discussion and analysis in proxy statements and reports filed under the Securities Exchange Act of 1934, as amended, or the Exchange Act, and instead provide a reduced level of disclosure concerning executive compensation.

We may take advantage of these reporting exemptions until we are no longer an “emerging growth company”, which in certain circumstances could be for up to five years. We will cease to be an “emerging growth company” upon the earliest of: (1) December 31, 2024; (2) the last day of the first fiscal year in which our annual gross revenue is $1.07 billion or more; (3) the date on which we have, during the previous rolling three-year period, issued more than $1 billion in non-convertible debt securities; and (4) the date on which we are deemed to be a “large accelerated filer” as defined in the Exchange Act.

With respect to the JOBS Act, we are taking advantage of some, but not all, of the reduced regulatory and reporting requirements that will be available to us so long as we qualify as an “emerging growth company.” We have elected to avail ourselves of this exemption and, therefore, we are not subject to the same new or revised accounting standards as other public companies that are not “emerging growth companies”. As a result, changes in rules of U.S. generally accepted accounting principles or their interpretation, the adoption of new guidance or the application of existing guidance to changes in our business could significantly affect our financial position and results of operations. In addition, our independent registered public accounting firm will not be required to provide an attestation report on the effectiveness of our internal control over financial reporting so long as we qualify as an “emerging growth company,” which may increase the risk that material weaknesses or significant deficiencies

in our internal control over financial reporting go undetected. Likewise, so long as we qualify as an “emerging growth company,” we may elect not to provide you with certain information, including certain financial information and certain information regarding compensation of our executive officers, that we would otherwise have been required to provide in filings we make with the SEC, which may make it more difficult for investors and securities analysts to evaluate our company. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock, and our stock price may be more volatile and may decline. In addition, if we lose our “emerging growth company” status sooner than anticipated, we may incur additional costs to comply with rules and regulations required for public companies, which may impact our financial position and results of operations.

Future changes in financial accounting standards or practices may cause adverse and unexpected revenue fluctuations and adversely affect our reported results of operations.

Future changes in financial accounting standards may cause adverse, unexpected revenue fluctuations and affect our reported financial position or results of operations. Financial accounting standards in the United States are constantly under review and new pronouncements and varying interpretations of pronouncements have occurred frequently in the past and are expected to occur again in the future. As a result, we may be required to make changes in our accounting policies. Those changes could affect our financial condition and results of operations or the way in which such financial condition and results of operations are reported. Compliance with new accounting standards may also result in additional expenses. As a result, we intend to invest all reasonably necessary resources to comply with evolving standards, and this investment may result in increased general and administrative expenses and a diversion of management time and attention from business activities to compliance activities.

We incur increased costs as a result of operating as a public company, and our management devotes substantial time to new compliance initiatives.

As a public company, we incur significant legal, accounting, insurance and other expenses that we did not incur as a private company, and these expenses may increase even more after we are no longer an “emerging growth company.” As a public company, we are subject to the reporting requirements of the Exchange Act, the Sarbanes-Oxley Act and the Dodd-Frank Act, as well as rules adopted, and to be adopted, by the SEC and the Nasdaq Global Select Market. Our management and other personnel devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations may increase our legal and financial compliance costs and may make some activities more time-consuming and costly. The increased costs will increase our net loss. For example, these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain sufficient coverage. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers.

Specifically, in order to comply with the requirements of being a public company, we need to undertake various actions, including implementing new internal controls and procedures and hiring new accounting or internal audit staff. The Sarbanes-Oxley Act requires that we maintain effective disclosure controls and procedures and internal control over financial reporting. We are continuing to develop and refine our disclosure controls and other procedures that are designed to ensure that information required to be disclosed by us in the reports that we file with the SEC is recorded, processed, summarized and reported within the time periods specified in the SEC’s rules and forms, and that information required to be disclosed in reports under the Exchange Act is accumulated and communicated to our principal executive and financial officers. Any failure to develop or maintain effective controls could adversely affect the results of periodic management evaluations. In the event that we are not able to demonstrate compliance with the Sarbanes-Oxley Act, that our internal control over financial reporting is perceived as inadequate or that we are unable to produce timely or accurate financial statements, investors may lose confidence in our operating results and the price of our common stock could decline. In addition, if we are unable to continue to meet these requirements, we may not be able to remain listed on the Nasdaq Global Select Market.

Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall.

Sales of a substantial number of shares of our 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 intend to sell shares, could reduce the market price of our common stock. Moreover, certain holders of our common stock have rights, subject to certain conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. Shares issued to Merck in the private placement that occurred concurrently with our IPO will be available for sale in the public market beginning on March 17, 2020, subject to the condition of Rule 144 under the Securities Act.

We do not intend to pay dividends on our common stock so any returns will be limited to the value of our stock.

We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will therefore be limited to the appreciation of their stock.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

We designed our disclosure controls and procedures to reasonably assure that information we must disclose in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well-conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

Some provisions of our charter documents, Delaware law and our agreement with Merck may have anti-takeover effects or could otherwise discourage an acquisition of us by others, even if an acquisition would benefit our stockholders, and may prevent attempts by our stockholders to replace or remove our current management.

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 to remove our current management. These provisions include:

- a board of directors divided into three classes serving staggered three-year terms, such that not all members of the board will be elected at one time;
- authorizing the issuance of “blank check” preferred stock, the terms of which we may establish and shares of which we may issue without stockholder approval;
- prohibiting cumulative voting in the election of directors, which would otherwise allow for less than a majority of stockholders to elect director candidates;
- prohibiting stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of our stockholders;
- eliminating the ability of stockholders to call a special meeting of stockholders; and

- establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings.

These provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, who are responsible for appointing the members of our management. Because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law ("DGCL") which may discourage, delay or prevent someone from acquiring us or merging with us whether or not it is desired by or beneficial to our stockholders. In addition, Section 203 of the DGCL prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder, which is generally a person that together with its affiliates owns, or within the last three years has owned, 15% of our voting stock, for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is approved in a prescribed manner.

Certain provisions in our agreement with Merck may also deter a change of control. For example, under our agreement with Merck, a change of control gives Merck the right to terminate our research and early development program as well as additional rights if our acquirer is a qualifying large pharmaceutical company or has a research, development or commercialization program that competes with a program optioned by Merck.

Any provision of our amended and restated certificate of incorporation, amended and restated bylaws, Delaware law or our agreement with Merck 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.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware and the federal district courts of the United States will be the exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for the following types of actions or proceedings under Delaware statutory or common law: any derivative action or proceeding brought on our behalf; any action asserting a breach of a fiduciary duty; any action asserting a claim against us arising pursuant to the DGCL, our amended and restated certificate of incorporation or our amended and restated bylaws; or any action asserting a claim against us that is governed by the internal affairs doctrine. This provision would not apply to claims brought to enforce a duty or liability created by the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction. Our amended and restated certificate of incorporation provides further that the federal district courts of the United States will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act, subject to and contingent upon a final adjudication in the State of Delaware of the enforceability of such exclusive forum provision. These choice of forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees. If a court were to find either choice of forum provision contained in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could harm our business. For example, in December 2018 the Court of Chancery of the State of Delaware determined that the exclusive forum provision of federal district courts of the United States for resolving any complaint asserting a cause of action arising under the Securities Act is not enforceable. However, this decision has been appealed to and may ultimately be overturned by the Delaware Supreme Court. If this ultimate adjudication were to occur, the federal district court exclusive forum provision in our amended and restated certificate of incorporation would no longer be applicable.

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.

Our stock price and trading volume is heavily influenced by the way analysts and investors interpret our financial information and other disclosures. If securities or industry analysts do not publish research or reports about our business, delay publishing reports about our business or publish negative reports about our business, regardless of accuracy, our stock price and trading volume could decline. The trading market for our common stock depends, in part, on the research and reports that securities or industry analysts publish about us or our business. We do not have any control over these analysts. A limited number of analysts are currently covering our company. If the number of analysts that cover us declines, demand for our common stock could decrease and our common stock price and trading volume may decline. Even if our common stock is actively covered by analysts, we do not have any control over the analysts or the measures that analysts or investors may rely upon to forecast our future results. Over-reliance by analysts or investors on any particular metric to forecast our future results may result in forecasts that differ significantly from our own.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

We lease and occupy approximately 122,000 square feet of laboratory and office space in South San Francisco, California. The lease is scheduled to expire in December 2023. We believe that our current spaces are adequate and suitable for our needs. We also believe we will be able to obtain additional space, as needed, on commercially reasonable terms.

Item 3. Legal Proceedings.

None.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

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

Market Information

Our common stock has been listed on the Nasdaq Global Select Market under the symbol "NGM" since April 4, 2019. Prior to that date, there was no public trading market for our common stock.

Holders of Record

As of the close of business on March 12, 2020, there were 78 stockholders of record of our common stock. The actual number of stockholders is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

Dividends

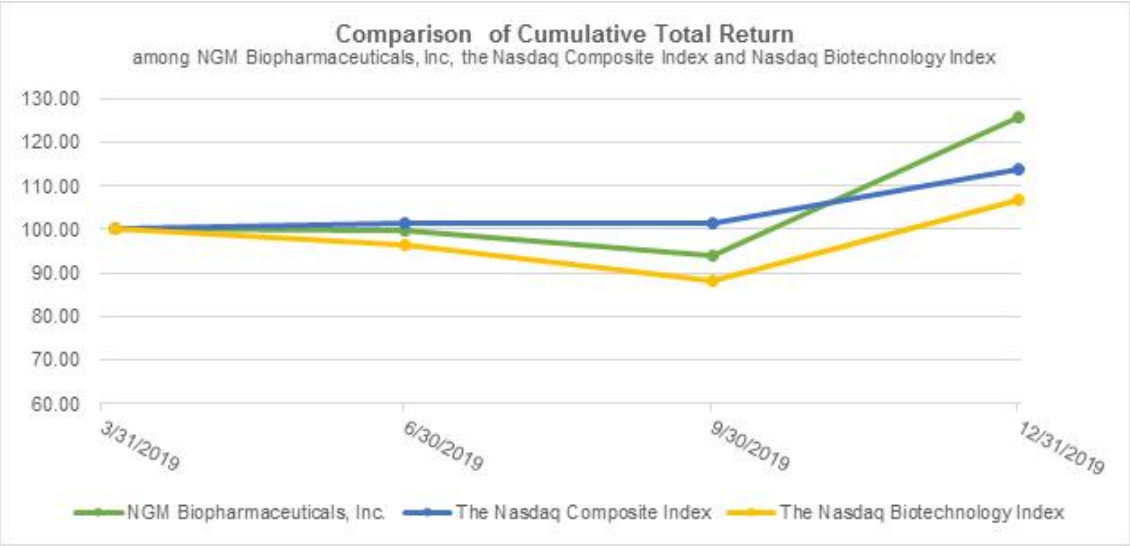
We have never declared or paid cash dividends on our common stock. We currently intend to retain all available funds and future earnings, if any, to fund the development and expansion of our business, and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination regarding the declaration and payment of dividends, if any, will be at the discretion of our board of directors and will depend on then-existing conditions, including our financial condition, operating results, contractual restrictions, capital requirements, business prospects and other factors our board of directors may deem relevant.

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.

Performance Graph

The following stock performance graph compares the value of an investment in (i) our common stock, (ii) Nasdaq Composite Index and (iii) Nasdaq Biotechnology Index for the period from April 4, 2019 (the date our common stock commenced trading on the Nasdaq Global Select Market) through December 31, 2019. The figures represented below assume an investment of $100 in our common stock at the closing price on April 4, 2019 and in the Nasdaq Composite Index and Nasdaq Biotechnology Index on April 4, 2019 and the reinvestment of dividends into shares of common stock. However, no dividends have been declared on our common stock to date. The comparisons in the table are required by the SEC and are not intended to forecast or be indicative of possible future performance of our common stock.



	4/4/2019	12/31/2019
NGM Biopharmaceuticals, Inc.	$ 100.00	$ 125.78
NASDAQ Composite Index	100.00	113.70
NASDAQ Biotechnology Index	100.00	106.66

The information under "Performance Graph" is not deemed to be "soliciting material" or "filed" with the SEC or subject to Regulation 14A or 14C, or to the liabilities of Section 18 of the Exchange Act, and is not to be incorporated by reference in any filing of NGM under the Securities Act or the Exchange Act, whether made before or after the date of this Annual Report and irrespective of any general incorporation language in those filings.

Recent Sales of Unregistered Securities

None.

Issuer Purchases of Equity Securities

None.

Use of Proceeds from our Public Offering of Common Stock

In April 2019, our Registration Statement on Form S-1 (No. 333-227608) was declared effective by the SEC and we issued and sold an aggregate of 7,521,394 shares of common stock (inclusive of 6,666,667 shares of common stock and 854,727 shares of common stock pursuant to the underwriters' exercise of their over-allotment option) at a public offering price of $16.00 per share for aggregate net cash proceeds of $107.8 million, after deducting underwriting discounts, commissions and offering costs. No payments for such expenses were made directly or indirectly to (i) any of our officers or directors or their associates, (ii) any persons owning 10% or more of any class of our equity securities or (iii) any of our affiliates.

The sale and issuance of 6,666,667 shares in the IPO closed on April 8, 2019 and the sale of 854,727 additional shares pursuant to the underwriters' over-allotment option closed on May 7, 2019. Goldman Sachs & Co. LLC, Citigroup Global Markets Inc. and Cowen and Company, LLC acted as joint book-running managers for the offering.

There has been no material change in the planned use of proceeds from the IPO from that described in the prospectus filed with the SEC pursuant to Rule 424(b)(4) under the Securities Act on April 4, 2019.

Item 6. Selected Consolidated Financial and Other Data.

The following selected consolidated financial and other data should be read in conjunction with, and are qualified by reference to, "*Management's Discussion and Analysis of Financial Condition and Results of Operations*," and our audited consolidated financial statements and the accompanying notes included elsewhere in this Annual Report. The consolidated statements of operations data for the fiscal years ended December 31, 2019, 2018 and 2017 and the consolidated balance sheets data as of December 31, 2019 and 2018 are derived from the audited consolidated financial statements that are included elsewhere in this Annual Report. The balance sheet data as of December 31, 2017 are derived from our audited consolidated financial statements not included in this Annual Report on Form 10-K. We have included, in our opinion, all adjustments, consisting only of normal recurring adjustments that we consider necessary for a fair presentation of the financial information set forth in those statements. Our historical results are not necessarily indicative of the results to be expected in any period in the future.

Consolidated Statements of Operations Data:

	Year Ended December 31,		
(in thousands, except share and per share amounts)	**2019**	**2018**	**2017**
Related party revenue	$ 103,544	$ 108,665	$ 77,141
Operating expenses:			
Research and development (1)	129,253	95,714	79,736
General and administrative (1)	23,631	17,265	14,830
Total operating expenses	152,884	112,979	94,566
Loss from operations	(49,340)	(4,314)	(17,425)
Interest income	6,692	3,622	2,358
Other income (expense), net	(147)	199	(152)
Net loss before taxes	(42,795)	(493)	(15,219)
Benefit from income taxes	—	—	(1,060)
Net loss	$ (42,795)	$ (493)	$ (14,159)
Net loss per share, basic and diluted	$ (0.85)	$ (0.08)	$ (2.37)
Weighted average shares used to compute net loss per share, basic and diluted (2)	50,297,524	6,383,751	5,961,767
Other comprehensive gain (loss), net of tax:			
Net unrealized gain (loss) on available-for-sale marketable securities	292	164	(329)
Total comprehensive loss	$ (42,503)	$ (329)	$ (14,488)

Consolidated Balance Sheets Data:

	As of December 31,		
(in thousands)	**2019**	**2018**	**2017**
Cash, cash equivalents and short-term marketable securities	$ 344,511	$ 206,633	$ 173,685
Working capital (excluding deferred revenue)	320,402	192,096	159,998
Total assets	380,403	246,085	248,941
Total liabilities	49,684	59,406	75,045
Convertible preferred stock warrant liability	—	198	121
Convertible preferred stock (2)	—	294,874	294,874
Accumulated deficit	(196,144)	(147,193)	(146,700)
Total stockholders' equity (deficit)	$ 330,719	$ (108,195)	$ (120,978)

(1) Includes stock-based compensation as follows:

	Year Ended December 31,		
(in thousands)	**2019**	**2018**	**2017**
Research and development	$ 7,278	$ 5,335	$ 4,723
General and administrative	5,584	4,524	2,994
Total stock-based compensation	$ 12,862	$ 9,859	$ 7,717

(2) In April 2019, we completed the IPO of our common stock in which we issued an aggregate of 7,521,394 shares of common stock for net proceeds of $107.8, after deducting underwriting discounts, commissions and offering costs. Upon the closing of our IPO, all of the outstanding shares of convertible preferred stock were converted into 47,283,839 shares of common stock.

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our consolidated financial statements and related notes appearing elsewhere in this Annual Report. This discussion contains forward-looking statements that reflect our plans, estimates and beliefs and involve risks and uncertainties. Our actual results and the timing of certain events could differ materially from those anticipated in these forward-looking statements as a result of several factors, including those discussed in the section titled "Risk Factors" included under Part I, Item 1A and elsewhere in this Annual Report. See "Special Note Regarding Forward-Looking Statements" in this Annual Report.

Overview

We are a clinical-stage biopharmaceutical company developing novel therapeutics based on our scientific understanding of key biological pathways underlying cardio-metabolic, liver, oncologic and ophthalmic diseases. These diseases represent leading causes of morbidity and mortality and a significant burden for healthcare systems. Since the commencement of our operations in 2008, we have generated a robust portfolio of product candidates. Our most advanced product candidate, aldafermin, previously known as NGM282, is wholly-owned and entered Phase 2b development for the treatment of NASH in 2019. Five of our other product candidates are in Phase 1 clinical trials and our other programs are in preclinical testing; some of these are subject to our Merck collaboration as described below.

In February 2015, we entered into a five-year research collaboration, product development and license agreement with Merck that allows us to develop multiple product candidates in parallel without bearing substantially greater costs or incurring significantly greater risk compared to developing candidates on our own. Through December 31, 2019, Merck had paid us $414.5 million, of which $20.0 million was to license NGM313 and related compounds and $394.5 million was upfront payment and reimbursement of research and development expenses. In March 2019, Merck exercised its option to extend the collaboration through March 16, 2022 and has the right to extend it again through March 16, 2024. As part of the extension through March 16, 2022, Merck agreed to continue to fund our research and development efforts at the same levels during the two-year extension period and, in lieu of a $20.0 million extension fee payable to us, Merck will make additional payments totaling up to $20.0 million in support of our research and development activities across 2021 and the first quarter of 2022.

In April 2019, we completed the IPO of our common stock, in which we issued an aggregate of 7,521,394 shares of common stock, including 854,727 shares of common stock issued pursuant to the over-allotment option granted to the underwriters, at a price of $16.00 per share, before underwriting discounts and commissions. We received approximately $107.8 million in net proceeds, after deducting underwriting discounts, commissions and offering expenses of $4.1 million, of which $2.2 million was paid in 2018. The deferred offering costs were offset against the net proceeds received from the sale of common stock. At the closing of the IPO, all shares of outstanding convertible preferred stock were automatically converted to 47,283,839 shares of common stock. Concurrent with the completion of the IPO, we also issued 4,121,683 shares of common stock to Merck in a private placement at a price of $16.00 per share for proceeds of $65.9 million, which resulted in Merck owning approximately 19.9% of our outstanding shares of common stock.

We have incurred net losses in each year since our inception. Our consolidated net losses were $42.8 million, $0.5 million and $14.2 million for the years ended December 31, 2019, 2018 and 2017, respectively. As of December 31, 2019, we had an accumulated deficit of $196.1 million, of which $6.1 million was a cumulative effect adjustment to accumulated deficit at January 1, 2019 for the adoption of Accounting Standards Update ("ASU") 2014-09, Revenue from Contracts with Customers (Topic 606), and subsequent amendments, under the modified retrospective approach. Substantially all of our net losses have resulted from costs incurred in connection with our research and development programs and general and administrative costs associated with our operations. Our net losses may fluctuate significantly from quarter to quarter and year to year, depending on the timing of our clinical trials and our expenses on other research and development activities.

Since inception, we have funded our operations primarily through the private placement of convertible preferred stock totaling $295.1 million, net proceeds from our IPO of $107.8 million, a private placement of shares of common stock to Merck for $65.9 million, research and development service fees provided by collaboration partners of $324.7 million, upfront license fees paid by collaboration partners of $123.0 million and the license of NGM313 and related compounds to Merck for $20.0 million. We do not have any products approved for sale and

do not anticipate generating revenue from product sales for the foreseeable future, if ever. We plan to continue to fund our operations and capital funding needs through public or private equity or debt financings, government or other third-party funding, collaborations, strategic alliances and licensing arrangements or a combination of these. The sale of convertible debt or additional equity could result in additional dilution to our stockholders. Incurring indebtedness would result in debt service obligations and could result in operating and financing covenants that would restrict our operations. We cannot assure you that financing will be available in the amounts we need or on terms acceptable to us, if at all. Our ability to raise additional capital may be adversely impacted by potential worsening global economic conditions and the recent disruptions to, and volatility in, the credit and financial markets in the United States and worldwide resulting from the ongoing COVID-19 pandemic. If we are not able to secure adequate additional funding, we may be forced to make reductions in spending, extend payment terms with suppliers, liquidate assets where possible and/or suspend or curtail planned programs. Any of these actions could materially harm our business, results of operations and future prospects. To the extent we obtain additional funding through product collaborations, these arrangements would generally require us to relinquish rights to some of our technologies, product candidates or products, and we may not be able to enter into such agreements on acceptable terms, if at all.

We have no manufacturing facilities and all of our manufacturing activities are contracted out to third parties. Additionally, we utilize third-party CROs to carry out certain clinical development activities.

Financial Operations Overview

Collaboration Revenue

Our revenue to date has been generated primarily from recognition of license fees and research and development service funding pursuant to our collaboration agreements, the most significant of which is with Merck. Merck is also a significant stockholder and, as such, collaboration revenue from Merck is referred to as related party revenue. We have not generated any revenue from commercial product sales to date. We receive research and development funding pursuant to our Collaboration Agreement and we may also be entitled to receive additional milestone and other contingent payments upon the occurrence of specific events. Due to the nature of this Collaboration Agreement and timing of related revenue recognition, our revenue has fluctuated from period to period in the past and we expect that it will continue to fluctuate in future periods.

The following table summarizes the sources of our collaboration revenue for the years ended December 31, 2019, 2018 and 2017 (in thousands):

	Year Ended December 31,		
	2019(1)	2018	2017
Related party revenue:			
Recognition of upfront fee	$ —	$ 18,800	$ 18,800
License revenue	—	20,000	—
Collaboration service revenue	103,544	69,865	58,341
Total related party revenue	$ 103,544	$ 108,665	$ 77,141

(1) We adopted ASU 2014-09, Revenue from Contracts with Customers (Topic 606), and subsequent amendments, under the modified retrospective approach on January 1, 2019. Refer to Note 2 to our consolidated financial statements for more details.

Research and Development Expenses

Research and development efforts relating to our product candidates include manufacturing drug substance, drug product and clinical trial materials, conducting preclinical testing and clinical trials and providing support for these operations.

Our research and development expenses consist of internal and external costs. Our internal costs include employee, consultant, facility and other research and development operating expenses. Our external costs include fees paid to CROs and other service providers in connection with our clinical trials and preclinical studies, third party license fees and costs related to acquiring and manufacturing drug substance, drug product and clinical trial materials.

Our clinical development efforts are focused on multiple programs. Our lead product candidate, aldafermin, is the subject of our recently completed Phase 2 and ongoing and planned Phase 2b clinical trials for NASH. We anticipate the majority of our financial resources outside of the Merck collaboration will be dedicated to the development of aldafermin for the foreseeable future. We are also devoting financial resources to the development of NGM395, a product candidate in our GDF15 receptor agonist program, and may devote financial resources to other programs in the event Merck does not elect to license these programs upon completion of a proof-of-concept study or in the event Merck elects to terminate its license to a program. Additionally, if our research and development expenses exceed the funding caps provided in our Collaboration Agreement, which we are anticipating in fiscal year ended December 31, 2020 and onwards, we could be required to devote our financial resources toward the development of programs subject to the collaboration.

The aldafermin clinical trials under our Phase 2 protocol include our recently completed 24-week expansion cohort of aldafermin (Cohort 4) as a double-blind, placebo-controlled study of once-daily 1 mg aldafermin for the treatment of patients with fibrosis stage F2 or F3 NASH. We have also initiated the ALPINE 2/3 clinical trial, which is a double-blind, placebo-controlled format testing 0.3 mg, 1 mg and 3 mg daily doses of aldafermin for 24 weeks for the treatment of patients with fibrosis stage F2 or F3 NASH, and plan to initiate the ALPINE 4 clinical trial of aldafermin for the treatment of F4 NASH patients with compensated cirrhosis in the first half of 2020. Significant portions of our research and development resources are focused on these clinical trials and other work needed to prepare aldafermin for potential regulatory approval for the treatment of NASH, including manufacturing of clinical trial materials and preparation for Phase 3 testing of aldafermin in NASH.

Our NGM313 product candidate has completed the SAD and MAD portions of Phase 1 testing in overweight or obese but otherwise healthy adults, as well as a Phase 1b study in obese insulin resistant subjects with NAFLD. Merck exercised its option to license the NGM313 program in 2018, and all future development expenses will be paid for by Merck unless we elect to exercise our worldwide cost and profit sharing option at the commencement of Phase 3 testing, at which point we would be responsible for a portion of the future development expense.

We have initiated Phase 1 clinical trials for NGM120, NGM217 and NGM621, each of which is subject to reimbursement under our Merck collaboration up to the funding caps provided in the Collaboration Agreement. We recently completed a Phase 1 trial assessing the safety, tolerability and pharmacokinetics of NGM120. This clinical trial demonstrated that NGM120 was well tolerated at all doses studied and the pharmacokinetics supported once-monthly dosing. Earlier this year, we initiated a Phase 1a/1b clinical study with NGM120 in cancer patients to explore its potential to treat cancer anorexia-cachexia syndrome and, possibly, tumors. Merck has a one-time option to license NGM120 following completion of a proof-of-concept study in humans.

We are also conducting a Phase 1 clinical trial of NGM217 to assess safety and tolerability and to inform dose-range finding for future studies. Thereafter, we plan to commence a Phase 1b/2a proof-of-concept study in diabetic patients to assess the ability of the agent to increase insulin production by the pancreas in the second half of 2020. Merck has a one-time option to license NGM217 following completion of a proof-of-concept study in humans.

We initiated a Phase 1 clinical trial of NGM621 in 2019 to assess the safety and tolerability of up to two intravitreal injections of NGM621 in patients with GA, the dry form of AMD. We also plan to initiate a Phase 2 proof-of-concept clinical trial in the second half of 2020. Merck has a one-time option to license NGM621 following completion of a proof-of-concept study in humans.

NGM395 and NGM386 comprise our GDF15 receptor agonist program and both were licensed to Merck at the inception of our collaboration. Substantially all of the related research and development expenses for these programs were borne directly by Merck under our Collaboration Agreement. Effective May 31, 2019, Merck terminated its license to the GDF15 receptor agonist program and we regained full rights to NGM395 and NGM386. Following our assessment of the NGM386 study results, we decided to suspend activities related to NGM386 and focus on advancing NGM395. We initiated a Phase 1 clinical trial to assess safety, tolerability and pharmacokinetics of NGM395 in obese but otherwise healthy adults in the first quarter of 2020. As a result, we will continue to incur research and development expenses with respect to NGM395 in the future.

Our research and development expenses related to the development of aldafermin, NGM313, NGM120, NGM217, NGM621 and NGM395 consist primarily of:

- fees paid to our CROs in connection with our clinical trials and other related clinical trial fees;
- costs related to acquiring and manufacturing drug substance, drug product and clinical trial materials, including continued testing, such as process validation and stability, of drug substance and drug product;
- costs related to toxicology testing and other research and preclinical related studies;
- salaries and related overhead expenses, which include stock-based compensation and benefits, for personnel in research and development functions;
- fees paid to consultants for research and development activities;
- research and development operating expenses, including facility costs and depreciation expenses; and
- costs related to compliance with regulatory requirements.

The process of conducting and supplying materials for preclinical studies and clinical trials necessary to obtain regulatory approval of our product candidates is costly and time consuming. We may never succeed in achieving marketing approval for our product candidates. The success of each product candidate may be affected by numerous factors, including preclinical data, clinical data, competition, manufacturing capability, our sales capabilities, our ability to work effectively with our collaboration partners, regulatory matters, third-party payor matters and commercial viability.

The following is a comparison of research and development expenses for our programs, including programs that are subject to our Collaboration Agreement with Merck, for the years ended December 31, 2019, 2018 and 2017 (in thousands):

	Year Ended December 31,		
	2019	2018	2017
External research and development expenses:			
Aldafermin (FGF19 analog)	$ 32,001	$ 15,359	$ 15,126
NGM313 (FGFR1c/KLB agonist)	2,009	3,544	3,948
NGM120 (GFRAL antagonist)	3,414	3,442	3,621
NGM217 (undisclosed)	2,139	2,808	3,764
NGM621 (C3 inhibitor)	4,420	6,791	186
NGM395 (GDF15 analog)	585	701	350
Other external research and development expenses	17,690	6,670	4,680
Total external research and development expenses	62,258	39,315	31,675
Personnel-related expenses	38,171	30,908	25,915
Internal and unallocated research and development expenses(1)	28,824	25,491	22,146
Total research and development expenses	$ 129,253	$ 95,714	$ 79,736

(1) Internal and unallocated research and development expenses consist primarily research supplies and consulting fees, which we deploy across multiple research and development programs.

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

- our ability to hire and retain key research and development personnel;
- whether Merck will elect to license or terminate its license to any of our programs and the timing of such election or termination;
- the scope, rate of progress, results and expense of our ongoing, as well as any additional, clinical trials and other research and development activities; and
- the timing and receipt of any regulatory approvals.

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

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation. Other significant costs include legal fees relating to patent and corporate matters, facility costs not otherwise included in research and development expenses and fees for accounting and other consulting services.

We anticipate that our general and administrative expenses will increase in the future to support our continued research and development activities. These increases will likely include increased costs related to the hiring of additional personnel and fees to outside consultants, lawyers and accountants, among other expenses. Additionally, we anticipate increased costs associated with being a public company, including expenses related to services associated with maintaining compliance with Nasdaq listing rules and related SEC requirements and insurance and investor relations costs. In addition, we may incur expenses associated with building a commercial organization in connection with, and prior to, potential future regulatory approval of our product candidates.

Results of Operations

Comparison of the Years Ended December 31, 2019 and 2018

The following table summarizes our results of operations for the years ended December 31, 2019 and 2018 (in thousands):

	Year Ended December 31,		
	2019	**2018**	**Change**
Related party revenue	$ 103,544	$ 108,665	$ (5,121)
Operating expenses:			
Research and development	129,253	95,714	33,539
General and administrative	23,631	17,265	6,366
Total operating expenses	152,884	112,979	39,905
Loss from operations	(49,340)	(4,314)	45,026
Interest income	6,692	3,622	3,070
Other income (expense), net	(147)	199	(346)
Net loss	$ (42,795)	$ (493)	$ 42,302

Related Party Revenue. Related party revenue was $103.5 million and $108.7 million for the years ended December 31, 2019 and 2018, respectively. The decrease of $5.1 million in revenue was primarily due to license revenue of $20.0 million related to NGM313 in 2018, partially offset by an increase of $9.7 million in reimbursable costs related to research personnel and research and development activities and an increase $5.2 million in upfront fee revenue due to the change in revenue recognition methodology associated with the adoption of ASC 606, which requires the recognition of revenue using the cost-based input method as opposed to ratable recognition under ASC 605, which was effective January 1, 2019.

Research and Development Expenses. Research and development expenses were $129.3 million and $95.7 million for the years ended December 31, 2019 and 2018, respectively. The increase in research and development expenses of $33.5 million was primarily attributable to an increase of $16.6 million in external expenses driven by ongoing clinical trials for our aldafermin program, $11.0 million for the acquisition of clinical trial materials, $7.3 million in personnel-related expenses due to increased headcount and $3.3 million in unallocated research and development expenses related to early research testing. These increases were partially offset by a decrease of $4.7 million in other program external expenses resulting from timing of clinical trial and manufacturing activities. We expect our research and development expenses to increase substantially in

connection with our ongoing activities, particularly to the extent that product candidates whose costs are not borne by our collaborator, such as aldafermin and NGM395, advance in clinical development.

General and Administrative Expenses. General and administrative expenses were $23.6 million and $17.3 million for the years ended December 31, 2019 and 2018, respectively. The increase in general and administrative expenses of $6.3 million was primarily attributable to an increase of $3.4 million in personnel-related expenses, including stock-based compensation due to increased headcount and the implementation of the 2019 Employee Stock Purchase Plan ("2019 ESPP"). Further increasing our general and administrative expenses were $2.0 million for consulting expenses, $1.3 million for legal and accounting expenses and $1.3 million in other miscellaneous general and administrative expenses, including supplies, travel and rent expenses. These increases were offset by $1.7 million in allocated overhead expenses from general and administrative expenses to research and development expenses. We anticipate general and administrative expenses will continue to increase year over year in connection with being a public company which may include increased expenses related to services associated with maintaining compliance with Nasdaq listing rules and related SEC requirements, insurance and investor relations costs.

Interest Income. Interest income was $6.7 million and $3.6 million for the years ended December 31, 2019 and 2018, respectively. The increase in interest income was primarily attributable to an increase in our cash and investments balance subsequent to the completion of our IPO and private placement in April 2019.

Comparison of the Years Ended December 31, 2018 and 2017

The following table summarizes our results of operations for the years ended December 31, 2018 and 2017 (in thousands):

	Year Ended December 31,		
	2018	2017	Change
Related party revenue	$ 108,665	$ 77,141	$ 31,524
Operating expenses:			
Research and development	95,714	79,736	15,978
General and administrative	17,265	14,830	2,435
Total operating expenses	112,979	94,566	18,413
Loss from operations	(4,314)	(17,425)	(13,111)
Interest income	3,622	2,358	1,264
Other income (expense), net	199	(152)	351
Net loss before taxes	(493)	(15,219)	(14,726)
Benefit from income taxes	—	(1,060)	(1,060)
Net loss	$ (493)	$ (14,159)	$ (13,666)

Related Party Revenue. Total related party revenue was $108.7 million and $77.1 million for the years ended December 31, 2018 and 2017, respectively, of which $18.8 million in both periods was related to the partial recognition of the upfront payment from Merck in 2015. The increase of $31.5 million in total revenue was due to an additional $20.0 million of revenue in 2018 recognized from the $20.0 million received from Merck to license NGM313 and related compounds and an increase in both reimbursable personnel related expenses and higher overall external research and development expenses that we incurred in 2018.

Research and Development Expenses. Research and development expenses were $95.7 million and $79.7 million for the years ended December 31, 2018 and 2017, respectively. The increase in research and development expenses of $16.0 million was primarily attributable to an increase of $9.2 million in external spend mainly driven by manufacturing costs of clinical materials related to our NGM621 program, $5.0 million in hiring- and personnel-related expenses and $3.3 million in unallocated research and development expenses related to early research testing. These increases were offset by a decrease of $1.5 million in external expense due to NGM217 program external expenses for manufacturing costs of clinical materials that occurred in 2017 and timing of clinical trial activities for our other programs.

General and Administrative Expenses. General and administrative expenses were $17.3 million and $14.8 million for the years ended December 31, 2018 and 2017, respectively. The increase in general and administrative expenses of $2.4 million was primarily due to an increase of $2.8 million in personnel-related expenses, $0.7 million for increased rent expense and increases in professional fees and contract services expenses, including $0.4 million for legal expenses and $0.4 million in audit and tax expenses. These increases were partially offset by $1.9 million in allocated overhead expenses from general and administrative expenses to research and development expenses.

Interest Income. Interest income was $3.6 million and $2.4 million for the years ended December 31, 2018 and 2017, respectively. The increase in interest income of $1.2 million was primarily attributable to higher yields on our available-for-sale marketable securities in 2018 compared to 2017.

Benefit from Income Taxes. Benefit from income taxes was zero and $1.1 million for the years ended December 31, 2018 and 2017, respectively. The benefit from income taxes in 2017 was due to a federal alternative minimum tax credit carryforward that became refundable as a result of the 2017 Tax Cuts and Jobs Act ("2017 Tax Act").

Liquidity and Capital Resources

We have incurred losses and negative cash flows from operating activities since our inception. To date, our operations have been financed primarily through the private placement of convertible preferred stock, research and development service fees provided by collaboration partners, primarily Merck, upfront license fees paid by collaboration partners and proceeds from our IPO and concurrent private placement in April 2019. As of December 31, 2019, we had cash and cash equivalents of $245.6 million, short-term marketable securities of $98.9 million, working capital (excluding deferred revenue) of $320.4 million and an accumulated deficit of $196.1 million.

We anticipate that we will continue to incur net losses for the foreseeable future as we continue the development of our product candidates, expand our corporate infrastructure to support operations as a public company and conduct pre-commercialization activities. We will require substantial additional capital to achieve our development and commercialization goals for our wholly-owned programs, aldafermin and NGM395, for any future programs that Merck does not opt to license under the Collaboration Agreement and that we choose to develop, for any Merck licensed programs that we opt to co-develop, and for any programs that Merck chooses to license under the Collaboration Agreement and later elects to terminate. Additionally, if our research and development expenses exceed the funding caps provided in our Collaboration Agreement, we could be required to devote our financial resources toward the development of programs subject to the collaboration. If our Merck collaboration were to be terminated, we would require significant additional capital in order to proceed with development and commercialization of our product candidates, or we may enter into additional collaboration or license agreements in order to fund such development and commercialization. We plan to continue to fund our operations and capital funding needs through public or private equity or debt financings, government or other third-party funding, collaborations, strategic alliances and licensing arrangements or a combination of these. The sale of convertible debt or additional equity could result in additional dilution to our stockholders. Incurring indebtedness would result in debt service obligations and could result in operating and financing covenants that would restrict our operations. We cannot assure you that financing will be available in the amounts we need or on terms acceptable to us, if at all. Our ability to raise additional capital may be adversely impacted by potential worsening global economic conditions and the recent disruptions to, and volatility in, the credit and financial markets in the United States and worldwide resulting from the ongoing COVID-19 pandemic. To the extent we obtain additional funding through product collaborations, these arrangements would generally require us to relinquish rights to some of our technologies, product candidates or products, and we may not be able to enter into such agreements on acceptable terms, if at all. If we are not able to secure adequate additional funding, we may be forced to make reductions in spending, extend payment terms with suppliers, liquidate assets where possible and/or suspend or curtail planned programs. Any of these actions could materially harm our business, results of operations and future prospects.

We believe that our existing cash and cash equivalents, along with amounts available to us under our Collaboration Agreement with Merck, will be sufficient to meet our anticipated cash requirements for at least the next 12 months. However, our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement that involves risks and uncertainties, and actual results could vary materially.

Cash Flows

The following table shows a summary of our cash flows for the years ended December 31, 2019, 2018 and 2017 (in thousands):

	Year Ended December 31,		
	2019	2018	2017
Net cash provided by (used in):			
Operating activities	$ (41,174)	$ (7,597)	$ (17,413)
Investing activities	48,723	38,729	(2,796)
Financing activities	180,751	198	339
Net increase (decrease) in cash and cash equivalents	$ 188,300	$ 31,330	$ (19,870)

Cash Used in Operating Activities

During the year ended December 31, 2019, cash used in operating activities was $41.2 million, which consisted of a net loss of $42.8 million, adjusted for non-cash charges of $19.6 million and cash used through changes in operating assets and liabilities of $17.9 million. The non-cash charges consisted primarily of stock-based compensation expense of $13.0 million and depreciation expense of $7.6 million. The change in operating assets and liabilities was mainly driven by an increase in related party receivable from collaboration of $1.5 million, increase in prepaid expenses and other current assets of $2.0 million, increase in accounts payable of $3.6 million and increase in accrued expenses and other current liabilities of $8.9 million. These increases were offset by a decrease in deferred rent of $2.7 million and deferred revenue of $24.2 million primarily attributed to both the changes in revenue recognition associated with the adoption of ASC 606 and the timing of advance payments from Merck related to the reimbursement of costs associated with research and development activities.

During the year ended December 31, 2018, cash used in operating activities was $7.6 million, which consisted of a net loss of $0.5 million, adjusted for non-cash charges of $16.5 million and cash used through changes in operating assets and liabilities of $23.6 million. The non-cash charges consisted primarily of stock-based compensation expense of $10.0 million and depreciation expense of $7.2 million. The change in operating assets and liabilities was primarily due to an increase in related party receivable from collaboration of $3.7 million under our agreement with Merck, increase in prepaid expenses and other current assets of $4.4 million, increase in accounts payable of $3.5 million and increase in accrued expenses and other current liabilities of $4.1 million. These increases were offset by a decrease in deferred rent and deferred revenue of $2.0 million and $21.1 million, respectively. The decrease in deferred revenue is primarily due to the recognition of upfront fees from Merck and the timing of advance payments from Merck related to the reimbursement of costs associated with research and development activities.

During the year ended December 31, 2017, cash used in operating activities was $17.4 million, which consisted of a net loss of $14.2 million, adjusted for non-cash charges of $14.5 million and cash used through changes in operating assets and liabilities of $17.7 million. The non-cash charges consisted primarily of stock-based compensation expense of $7.7 million and depreciation expense of $6.4 million. The change in operating assets and liabilities was primarily due to an increase in prepaid expenses and other current assets of $1.1 million primarily resulting from a federal tax receivable generated as a result of the 2017 Tax Act that was signed into law in December 2017 and increase in accrued expenses and other current liabilities of $2.6 million resulting from the timing of payments related to our clinical trial expenses and other research and development activities. These increases were offset by a decrease in related party receivable from collaboration of $2.8 million due to payments received from Merck under the Collaboration Agreement, decrease in accounts payable of $4.2 million, decrease in deferred rent of $1.3 million and decrease in deferred revenue of $16.5 million due to the recognition of revenue related to upfront fees from Merck and the timing of advance payments from Merck related to the reimbursement of costs associated with research and development activities.

Cash Provided by Investing Activities

During the year ended December 31, 2019, cash provided by investing activities was $48.7 million, which consisted of $186.5 million in proceeds from the maturities of marketable securities, partially offset by purchases of marketable securities of $134.3 million and purchases of property and equipment of $3.5 million.

During the year ended December 31, 2018, cash provided by investing activities was $38.7 million, which consisted of $178.2 million in proceeds from the maturities of marketable securities, partially offset by purchases of marketable securities of $133.6 million and purchases of property and equipment of $5.8 million.

During the year ended December 31, 2017, cash used in investing activities was $2.8 million, which consisted of $217.3 million in purchases of marketable securities and purchases of property and equipment of $6.4 million, partially offset by proceeds from the maturities of marketable securities of $220.9 million.

Cash Provided by Financing Activities

During the year ended December 31, 2019, cash provided by financing activities was $180.8 million, which consisted of net proceeds from issuance of common stock upon completion of our IPO of $110.0 million, issuance of common stock upon completion of the private placement with Merck of $65.9 million, issuance of common stock upon the exercise of previously granted stock options of $3.6 million and issuance of common stock in connection with our 2019 ESPP of $1.3 million. The net proceeds received from the completion of our IPO of $110.0 million included proceeds, after deducting underwriting discounts and commissions, of $111.9 million less offering expenses of $4.1 million, of which $2.2 million was paid in 2018.

During the year ended December 31, 2018, cash provided by financing activities was $0.2 million, which consisted proceeds from the issuance of common stock upon the exercise of previously granted stock options of $2.6 million less deferred IPO costs of $2.2 million and repurchases of common stock of $0.2 million.

During the year ended December 31, 2017, cash provided by financing activities was $0.3 million, which consisted of proceeds from the issuance of common stock upon the exercise of previously granted stock options.

Off-Balance Sheet Arrangements

We currently have not entered into and do not have any relationships with unconsolidated entities or financial collaborations, such as entities often referred to as structured finance or special purpose entities, which would have been established for the purpose of facilitating off-balance sheet arrangements or other contractually narrow or limited purpose.

Contractual Obligations

Our principal obligations consist of the operating lease for our facilities and non-cancelable purchase commitments with contract manufacturers or service providers. The following table sets out, as of December 31, 2019, our contractual obligations due by period (in thousands):

	Payments due by period				
	Less than 1 year	1 to 3 years	4 to 5 years	More than 5 years	Total
Contractual obligations:					
Operating lease obligations[1]	$ 4,995	$ 15,890	$ —	$ —	$ 20,885
Total contractual obligations	$ 4,995	$ 15,890	$ —	$ —	$ 20,885

(1) Consists of our corporate headquarters lease encompassing approximately 122,000 square feet of office and laboratory space that expires in December 2023.

We enter into agreements in the normal course of business with CROs, contract manufacturers and with vendors for preclinical studies and other services and products for operating purposes that are generally cancelable at any time by us, upon prior written notice, and may or may not include cancellation fees. Given that the amount and timing related to such payments are uncertain, they have not been included in the table above.

We are obligated to make future payments to third parties under in-license agreements, including sublicense fees, low single-digit royalties and payments that become due and payable on the achievement of certain development and commercialization milestones. As the amount and timing of sublicense fees and the achievement and timing of these milestones are not probable and estimable, such commitments have not been included on our consolidated balance sheets or in the contractual obligations table above.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which we have prepared in accordance with United States generally accepted accounting principles ("U.S. GAAP"). The preparation of our 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 our consolidated financial statements, as well as revenue and expenses during the reported periods. We evaluate these estimates and judgments on an ongoing basis. We base our estimates on 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 materially from these estimates under different assumptions or conditions.

Our significant accounting policies are described in *Note 2* to our consolidated financial statements appearing elsewhere in this Annual Report. We believe that the following accounting policies are the most critical for fully understanding and evaluating our financial condition and results of operations.

Revenue Recognition

On January 1, 2019, we adopted ASU 2014-09, Revenue from Contracts with Customers (Topic 606), and subsequent amendments, using the modified retrospective transition method applied to those contracts that were not completed as of January 1, 2019. ASC 606 supersedes all prior revenue recognition guidance. Results for operating periods beginning after January 1, 2019 are presented under ASC 606, while prior period amounts have not been adjusted and continue to be reported in accordance with previous accounting rules under ASC 605.

Prior to the adoption of ASC 606, our revenue from collaboration agreements was recognized when we determined that persuasive evidence of an arrangement exists, services had been rendered, the price was fixed or determinable and collectability was reasonably assured. We would record amounts received prior to satisfying the above revenue recognition criteria as deferred revenue until all applicable revenue recognition criteria were met. Revenue allocated to research activities was generally recognized in the period the services were performed, and revenue allocated to licenses was generally recognized on a straight-line basis over the contractual term. Allocations to non-contingent elements were based on the relative selling price of each element using vendor-specific objective evidence or third-party evidence, where available. In the absence of either of these measures, we used the best estimate of selling price for that deliverable.

The most significant change to our policies upon the adoption of ASC 606 is the estimation of an arrangement's total transaction price, which includes unconstrained variable consideration, and the recognition of that transaction price based on a cost-based input method that requires estimates to determine, at each reporting period, the percentage of completion based on the estimated total effort required to complete the project and the total transaction price. Given the differences in revenue recognition policies, the revenue recognized in prior years is not strictly comparable to revenue recorded in the year ending December 31, 2019 or in future periods (see *Recently Adopted Accounting Pronouncements* in the consolidated financial statements).

The core principle in ASC 606 requires an entity to recognize revenue upon the transfer of goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. We apply the following five-step revenue recognition model outlined in ASC 606 to adhere to this core principle: (1) identify the contract(s) with a customer; (2) identify the performance obligations in the contract; (3) determine the transaction price; (4) allocate the transaction price to the performance obligations in the contract; and (5) recognize revenue when (or as) we satisfy a performance obligation.

All of our revenue to date has been generated from our collaboration agreements, primarily our Collaboration Agreement. The terms of these agreements generally require us to provide (i) license options for our compounds, (ii) research and development services and (iii) non-mandatory services in connection with participation in research or steering committees. Payments received under these arrangements may include non-refundable upfront license fees, partial or complete reimbursement of research and development costs, contingent consideration payments based on the achievement of defined collaboration objectives and royalties on sales of commercialized products. In some agreements, the collaboration partner is solely responsible for meeting defined objectives that trigger contingent or royalty payments. Often the partner only pursues such objectives subsequent to exercising an optional license on compounds identified as a result of the research and development services performed.

We assess whether the promises in our arrangements, including any options provided to the customer, are considered distinct performance obligations that should be accounted for separately. Judgment is required to determine whether the license to a compound is distinct from research and development services or participation in steering committees, as well as whether options create material rights in the contract.

The transaction price in each arrangement is generally comprised of a non-refundable upfront fee and unconstrained variable consideration related to the performance of research and development services. We typically submit a budget for the research and development services to the customer in advance of performing the services. The transaction price is allocated to the identified performance obligations based on the standalone selling price (“SSP”) of each distinct performance obligation. Judgment is required to determine SSP. In instances where SSP is not directly observable, such as when a license or service is not sold separately, SSP is determined using information that may include market conditions and other observable inputs. We utilize judgment to assess the nature of our performance obligations to determine whether they are satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress toward completion. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

Our collaboration agreements may include contingent payments related to specified development and regulatory milestones or contingent payments for royalties based on sales of a commercialized product. Milestones can be achieved for such activities in connection with progress in clinical trials, regulatory filings in various geographical markets and marketing approvals from regulatory authorities. Sales-based royalties are generally related to the volume of annual sales of a commercialized product. At the inception of each agreement that includes such payments, we evaluate whether the milestones are considered probable of being achieved and estimate the amount to be included in the transaction price by using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within our or our customer’s control, such as those related to regulatory approvals, are not considered probable of being achieved until those approvals are received. The transaction price is then allocated to each performance obligation based on a relative SSP basis. At the end of each subsequent reporting period, we re-evaluate the probability of achievement of each such milestone and any related constraint and, if necessary, adjust our estimate of the overall transaction price. Pursuant to the guidance in ASC 606, sales-based royalties are not included in the transaction price. Instead, royalties are recognized at the later of when the performance obligation is satisfied or partially satisfied, or when the sale that gives rise to the royalty occurs.

Accrued Research and Development Expenses

As part of the process of preparing these consolidated financial statements, we are required to estimate and accrue expenses, the largest of which are research and development expenses. This process involves:

- Identifying services that have been performed on our behalf by third-party vendors and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual cost;
- estimating and accruing expenses in our consolidated financial statements as of each balance sheet date based on facts and circumstances known to us at the time; and
- periodically confirming the accuracy of our estimates with selected service providers and making adjustments, if necessary.

Examples of estimated research and development expenses that we accrue include:

- fees paid to CROs in connection with preclinical studies and clinical trials;
- fees paid to investigative sites in connection with clinical trials;
- fees paid to CMOs in connection with the production of clinical trial materials; and
- professional service fees for consulting and other services.

We base our expense accruals related to clinical trials on our estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and CROs that conduct and manage clinical trials on our behalf. The financial terms of these agreements vary from contract to contract and may result in uneven payment flows. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical study milestones. Our service providers generally invoice us monthly in arrears for services performed. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If we do not identify costs that we have begun to incur or if we underestimate or overestimate the level of services performed or the costs of these services, our actual expenses could differ from our estimates.

All of our clinical trials have been executed with support from CROs and other vendors. We accrue costs for clinical trial activities performed by CROs based upon the estimated amount of work completed on each trial. For clinical trial expenses, the significant factors used in estimating accruals include the number of patients enrolled, the activities to be performed for each patient, the number of active clinical sites and the duration for which the patients will be enrolled in the trial. We monitor patient enrollment levels and related activities to the extent possible through internal reviews, correspondence with CROs and review of contractual terms. We base our estimates on the best information available at the time.

To date, we have not experienced significant changes in our estimates of accrued research and development expenses after a reporting period. However, due to the nature of estimates, we cannot assure that we will not make changes to our estimates in the future as we become aware of additional information about the status or conduct of our clinical trials and other research activities.

Stock-Based Compensation

Stock-based compensation expense represents the grant-date fair value of employee stock option granted under our 2008 Equity Incentive Plan (the “2008 Plan”) and 2018 Equity Incentive Plan (the “2018 Plan”) and rights to acquire stock granted under our 2019 ESPP, recognized over the requisite service period of the awards (usually the vesting period) on a straight-line basis, net of estimated forfeitures.

On January 1, 2019, we adopted ASU 2018-07, Compensation – Stock Compensation (Topic 718): Improvements to Non-Employee Share-Based Payment Accounting. Subsequent to the adoption of ASU 2018-07, stock-based compensation expense for non-employee stock-based awards is also measured based on the fair value on grant date with its estimated fair value recorded over the requisite service period of the awards (usually the vesting period) on a straight-line basis, net of estimated forfeitures.

We calculate the fair value of stock-based compensation awards using the Black-Scholes option-pricing model. The Black-Scholes option-pricing model requires the use of subjective assumptions, including stock price volatility, the expected life of stock options, risk free interest rate and the fair value of the underlying common stock on the date of grant. Our key assumptions are:

- ***Expected Stock Price Volatility:*** The expected volatility is based on the historical volatility of the common stock of similar entities within our industry over periods commensurate with our expected term assumption.
- ***Expected Term of Options:*** The expected term of options represents the period of time options are expected to be outstanding. The expected term of the options granted is derived using the "simplified" method (that is, estimating the expected term as the mid-point between the vesting date and the end of the contractual term for each option).
- ***Risk-free Interest Rate:*** We base the risk-free interest rate on the interest rate payable on U.S. Treasury securities in effect at the time of grant for a period that is commensurate with the assumed expected option term.
- ***Expected Annual Dividends:*** The estimate for annual dividends is zero because we have not historically paid dividends and do not expect to pay dividends for the foreseeable future.

We recorded stock-based compensation expense related to employees, directors and nonemployees of $12.9 million, $9.9 million and $7.7 million for the years ended December 31, 2019, 2018 and 2017, respectively. As of December 31, 2019, we had unrecognized stock-based compensation cost related to options granted to employees and directors of $24.1 million, net of forfeitures, which is expected to be recognized as expense over approximately 2.67 years.

Prior to the closing of the Company's IPO, the fair value of the common stock underlying our share-based awards was estimated on each grant date by our board of directors. In order to determine the fair value of our common stock underlying option grants, our board of directors considered, among other things, timely valuations of our common stock prepared by an unrelated third-party valuation firm in accordance with the guidance provided by the American Institute of Certified Public Accountants ("AICPA") Practice Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*. Given the absence of a public trading market for our common stock historically, our board of directors exercised reasonable judgment and considered a number of objective and subjective factors to determine the best estimate of the fair value of our common stock, including our stage of development; progress of our research and development efforts; the rights, preferences and privileges of our convertible preferred stock relative to those of our common stock; equity market conditions affecting comparable public companies; and the lack of marketability of our common stock.

After our IPO, the fair market value of each share of underlying common stock is determined based on the closing price of our common stock as reported by the Nasdaq Global Select Market on the date of grant.

JOBS Act Accounting Election

We are an "emerging growth company," as defined in the JOBS Act. Under the JOBS Act, emerging growth companies may delay the adoption of new or revised accounting standards issued subsequent to the enactment of the JOBS Act until such time as those standards would otherwise apply to private companies.

The JOBS Act permits an "emerging growth company" such as us to take advantage of an extended transition time to comply with new or revised accounting standards as applicable to public companies. We have elected the extended transition period for complying with new or revised accounting standards pursuant to Section 107(b) of the JOBS Act until the earlier of the date we (i) are no longer an emerging growth company or (ii) affirmatively and irrevocably opt out of the extended transition period provided in the JOBS Act. As a result, our financial statements may not be comparable to companies that comply with new or revised accounting pronouncements as of public company effective dates.

We will remain an emerging growth company until the earlier to occur of (1) (a) December 31, 2024, (b) the last day of the fiscal year in which our annual gross revenue is $1.07 billion or more, or (c) the date on which we are deemed to be a "large-accelerated filer," under the rules of the SEC, which means the market value of our equity

securities that is held by non-affiliates exceeds $700 million as of the prior June 30th, and (2) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

Newly Issued Accounting Pronouncements

Refer to *Note 2* of our consolidated financial statements included elsewhere in this Annual Report on Form 10-K for a summary of recently issued and adopted accounting pronouncements.

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

We are exposed to market risks in the ordinary course of our business, primarily related to interest rate and foreign currency sensitivities.

Interest Rate Sensitivity

We are exposed to market risk related to changes in interest rates. We had cash, cash equivalents and marketable securities of $344.5 million as of December 31, 2019, which consisted primarily of money market funds and marketable securities, largely composed of investment grade, short to intermediate term fixed income securities.

The primary objective of our investment activities is to preserve capital to fund our operations. We also seek to maximize income from our investments without assuming significant risk. To achieve our objectives, we maintain a portfolio of investments in a variety of securities of high credit quality and short-term duration, according to our board-approved investment charter. Our investments are subject to interest rate risk and could fall in value if market interest rates increase. A hypothetical 10% relative change in interest rates during any of the periods presented would not have had a material impact on our consolidated financial statements.

Foreign Currency Sensitivity

The majority of our transactions occur in U.S. Dollars. However, we do have certain transactions that are denominated in currencies other than the U.S. Dollar, primarily British Pounds, Swiss Francs, Australian dollars and the Euro, and we therefore are subject to foreign exchange risk. The fluctuation in the value of the U.S. Dollar against other currencies affects the reported amounts of expenses, assets and liabilities associated with a limited number of manufacturing, preclinical and clinical activities. A hypothetical 10% change in foreign currency exchange rates during any of the periods presented would not have had a material impact on our consolidated financial statements.

Item 8. Financial Statements and Supplementary Data.

NGM BIOPHARMACEUTICALS, INC.
INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and the Board of Directors of
NGM Biopharmaceuticals, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of NGM Biopharmaceuticals, Inc. (the Company) as of December 31, 2019 and 2018, and the related consolidated statements of operations, comprehensive loss, convertible preferred stock and stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2019, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 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 U.S. generally accepted accounting principles.

Adoption of ASU No. 2014-09

As discussed in Note 2 to the consolidated financial statements, the Company changed its method for recognizing revenue as a result of the adoption of Accounting Standards Update No. 2014-09, Revenue from Contracts with Customers (Topic 606), effective January 1, 2019.

Basis for Opinion

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

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

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

Redwood City, California
March 17, 2020

NGM BIOPHARMACEUTICALS, INC.
CONSOLIDATED BALANCE SHEETS
(In thousands, except share amounts)

	December 31, 2019	December 31, 2018
Assets		
Current assets:		
Cash and cash equivalents	$ 245,598	$ 56,923
Short-term marketable securities	98,913	149,710
Related party receivable from collaboration	5,206	3,669
Prepaid expenses and other current assets	5,531	4,255
Total current assets	355,248	214,557
Non-current assets:		
Property and equipment, net	19,475	23,893
Restricted cash	1,874	2,249
Deferred IPO costs	—	2,292
Other non-current assets	3,806	3,094
Total assets	$ 380,403	$ 246,085
Liabilities, convertible preferred stock and stockholders' equity (deficit)		
Current liabilities:		
Accounts payable	$ 9,026	$ 5,775
Accrued liabilities	22,991	14,003
Deferred rent, current	2,829	2,683
Deferred revenue, current	4,872	19,025
Total current liabilities	39,718	41,486
Deferred rent, non-current	9,392	12,221
Deferred revenue, non-current	—	3,942
Early exercise stock option liability	574	1,559
Convertible preferred stock warrant liability	—	198
Total liabilities	49,684	59,406
Commitments and contingencies (Note 7)		
Convertible preferred stock, $0.001 par value; 96,268,206 shares authorized; zero and 47,267,466 shares issued and outstanding as of December 31, 2019 and 2018, respectively	—	294,874
Stockholders' equity (deficit):		
Preferred stock, $0.001 par value; 10,000,000 shares authorized; no shares issued or outstanding as of December 31, 2019 and 2018, respectively	—	—
Common stock, $0.001 par value; 400,000,000 shares authorized; 66,960,279 and 6,937,890 shares issued and outstanding as of December 31, 2019 and 2018, respectively	67	7
Additional paid-in capital	526,771	39,258
Accumulated other comprehensive gain (loss)	25	(267)
Accumulated deficit	(196,144)	(147,193)
Total stockholders' equity (deficit)	330,719	(108,195)
Total liabilities, convertible preferred stock and stockholders' equity (deficit)	$ 380,403	$ 246,085

See accompanying notes to consolidated financial statements.

NGM BIOPHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS
(In thousands, except share and per share amounts)

	Year Ended December 31,		
	2019	**2018**	**2017**
Related party revenue	$ 103,544	$ 108,665	$ 77,141
Operating expenses:			
Research and development	129,253	95,714	79,736
General and administrative	23,631	17,265	14,830
Total operating expenses	152,884	112,979	94,566
Loss from operations	(49,340)	(4,314)	(17,425)
Interest income	6,692	3,622	2,358
Other income (expense), net	(147)	199	(152)
Net loss before taxes	(42,795)	(493)	(15,219)
Benefit from income taxes	—	—	(1,060)
Net loss	$ (42,795)	$ (493)	$ (14,159)
Net loss per share, basic and diluted	$ (0.85)	$ (0.08)	$ (2.37)
Weighted average shares used to compute net loss per share, basic and diluted	50,297,524	6,383,751	5,961,767

See accompanying notes to consolidated financial statements.

NGM BIOPHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS
(In thousands)

	Year Ended December 31,		
	2019	**2018**	**2017**
Net Loss	$ (42,795)	$ (493)	$ (14,159)
Other comprehensive gain (loss), net of tax:			
Net unrealized gain (loss) on available-for-sale marketable securities	292	164	(329)
Total comprehensive loss	$ (42,503)	$ (329)	$ (14,488)

See accompanying notes to consolidated financial statements.

NGM BIOPHARMACEUTICALS, INC.
CONSOLIDATED CONVERTIBLE PREFERRED STOCK
AND STOCKHOLDERS' EQUITY (DEFICIT)
(In thousands)

	Convertible Preferred Stock		Common Stock		Additional Paid-In	Other Comprehensive	Accumulated	Total Stockholders'
	Shares	Amount	Shares	Amount	Capital	Gain (Loss)	Deficit	Equity(Deficit)
Balance at December 31, 2016	47,267	$ 294,874	5,802	$ 6	$ 17,575	$ (102)	$ (132,541)	$ (115,062)
Issuance of common stock to participants in 401(k) Plan	—	—	10	—	82	—	—	82
Issuance of common stock upon exercise of stock options	—	—	109	—	339	—	—	339
Vesting of common stock from early exercises	—	—	184	—	527	—	—	527
Stock-based compensation expense	—	—	—	—	7,624	—	—	7,624
Changes in unrealized loss on available-for-sale securities	—	—	—	—	—	(329)	—	(329)
Net loss	—	—	—	—	—	—	(14,159)	(14,159)
Balance at December 31, 2017	47,267	$ 294,874	6,105	$ 6	$ 26,147	$ (431)	$ (146,700)	$ (120,978)
Issuance of common stock to participants in 401(k) Plan	—	—	11	—	91	—	—	91
Issuance of common stock upon exercise of stock options	—	—	479	1	2,582	—	—	2,583
Vesting of common stock from early exercises	—	—	161	—	764	—	—	764
Repurchase of common stock	—	—	(23)	—	(185)	—	—	(185)
Stock-based compensation expense	—	—	—	—	9,859	—	—	9,859
Changes in unrealized gain on available-for-sale securities	—	—	—	—	—	164	—	164
Net loss	—	—	—	—	—	—	(493)	(493)
Balance at December 31, 2018	47,267	$ 294,874	6,733	$ 7	$ 39,258	$ (267)	$ (147,193)	$ (108,195)
Cumulative effect adjustment upon adoption of ASU 2014-09	—	—	—	—	—	—	(6,156)	(6,156)
Net exercise of preferred stock warrant to Series A preferred stock	16	198	—	—	—	—	—	—
Conversion of Series A, B, C, D, E convertible preferred stock to common stock concurrent with initial public offering	(47,283)	(295,072)	47,283	47	295,025	—	—	295,072
Issuance of common stock upon initial public offering, net of issuance cost	—	—	7,521	8	107,748	—	—	107,756
Issuance of common stock upon private placement	—	—	4,122	4	65,943	—	—	65,947
Issuance of common stock to participants in 401(k) Plan	—	—	8	—	98	—	—	98
Issuance of common stock upon exercise of stock options	—	—	984	1	3,574	—	—	3,575
Issuance of common stock in connection with employee stock purchase plan	—	—	103	—	1,270	—	—	1,270
Vesting of common stock from early exercises	—	—	132	—	993	—	—	993
Stock-based compensation expense	—	—	—	—	12,862	—	—	12,862
Changes in unrealized gain on available-for-sale securities	—	—	—	—	—	292	—	292
Net loss	—	—	—	—	—	—	(42,795)	(42,795)
Balance at December 31, 2019	—	—	66,886	$ 67	$ 526,771	$ 25	$ (196,144)	$ 330,719

See accompanying notes to consolidated financial statements.

NGM BIOPHARMACEUTICALS, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

	Year Ended December 31,		
	2019	**2018**	**2017**
Cash flows from operating activities			
Net loss	$ (42,795)	$ (493)	$ (14,159)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation	7,605	7,223	6,441
Amortization of discount on marketable securities	(1,123)	(876)	241
Stock-based compensation expense	12,981	9,962	7,717
Change in fair value of convertible preferred stock warrant liability	—	77	3
Other non-cash expenses	98	91	82
Changes in operating assets and liabilities:			
Related party receivable from collaboration	(1,537)	(3,669)	2,769
Prepaid expenses and other assets	(1,988)	(4,365)	(1,103)
Accounts payable	3,642	3,484	(4,230)
Accrued expenses and other liabilities	8,877	4,059	2,603
Deferred rent	(2,683)	(1,957)	(1,256)
Deferred revenue	(24,251)	(21,133)	(16,521)
Net cash used in operating activities	(41,174)	(7,597)	(17,413)
Cash flows from investing activities			
Purchase of marketable securities	(134,306)	(133,609)	(217,291)
Proceeds from sales and maturities of marketable securities	186,518	178,182	220,917
Purchase of property and equipment	(3,489)	(5,844)	(6,422)
Net cash provided by (used in) investing activities	48,723	38,729	(2,796)
Cash flows from financing activities			
Proceeds from issuance of common stock upon initial public offering, net of issuance costs	109,959	—	—
Proceeds from issuance of common stock upon completion of private placement	65,947	—	—
Proceeds from issuance of common stock upon exercise of stock options	3,575	2,583	339
Proceeds from issuance of common stock in connection with employee stock purchase plan	1,270	—	—
Repurchase of common stock	—	(185)	—
Deferred IPO costs	—	(2,200)	—
Net cash provided by financing activities	180,751	198	339
Net increase (decrease) in cash and cash equivalents	188,300	31,330	(19,870)
Cash, cash equivalents and restricted cash at beginning of period	59,172	27,842	47,712
Cash, cash equivalents and restricted cash at end of period	$ 247,472	$ 59,172	$ 27,842
Reconciliation of cash, cash equivalents and restricted cash to the consolidated balance sheets:			
Cash and cash equivalents	$ 245,598	$ 56,923	$ 25,593
Restricted cash	1,874	2,249	2,249
Total cash, cash equivalents and restricted cash	$ 247,472	$ 59,172	$ 27,842
Supplemental disclosures of cash flow information:			
Income taxes paid	$ —	$ 1	$ 536
Non-cash investing and financing activities:			
Net exercise of convertible preferred stock warrant to Series A preferred stock	$ 198	$ —	$ —
Vesting of common stock from early exercises	993	764	527
Cost of property and equipment in accounts payable and accrued liabilities	305	607	208
Deferred IPO costs in accounts payable and accrued liabilities	$ —	$ 92	$ —

See accompanying notes to consolidated financial statements.

1. Organization and Description of Business

NGM Biopharmaceuticals, Inc. and its wholly-owned subsidiary (collectively, referred to as the "Company") is a research-driven, clinical-stage biopharmaceutical company committed to discovering and developing first-in-class therapeutics for major diseases with an initial focus on cardio-metabolic, liver, oncologic and ophthalmic diseases. The Company's current portfolio is composed of six product candidates (aldafermin (NGM282), NGM313, NGM120, NGM217, NGM621 and NGM395) focused on NASH, diabetes, oncology, AMD and metabolic disease.

The Company was incorporated in Delaware in December 2007 and its headquarters are located at 333 Oyster Point Blvd., South San Francisco, California 94080. The Company operates in one business segment.

Stock Split

On March 22, 2019, the Company filed an amendment to the Company's amended and restated certificate of incorporation to effect a reverse split of shares of the Company's common stock on a two-for-one basis (the "Reverse Stock Split"). In connection with the Reverse Stock Split, the conversion ratio for the Company's outstanding convertible preferred stock was proportionately adjusted such that the common stock issuable upon conversion of such preferred stock was decreased in proportion to the Reverse Stock Split. The par value of the common stock was not adjusted as a result of the Reverse Stock Split. All references to common stock, options to purchase common stock, early exercised options, share data, per share data, convertible preferred stock (to the extent presented on an as-converted to common stock basis) and related information contained in these consolidated financial statements have been retrospectively adjusted to reflect the effect of the Reverse Stock Split for all periods presented.

Initial Public Offering

On April 3, 2019, the Company's registration statement on the Form S-1 was declared effective by the SEC for its IPO of its common stock. The Company's shares of common stock started trading on the Nasdaq Global Select Market on April 4, 2019 and the transaction closed on April 8, 2019. In connection with the IPO, the Company sold an aggregate of 7,521,394 shares of common stock, which included 6,666,667 shares of common stock and 854,727 shares of common stock sold pursuant to the underwriters' exercise of their option to purchase additional shares, at a public offering price of $16.00 per share. The aggregate net proceeds received by the Company from the offering were $107.8 million, net of underwriting discounts and commissions as well as offering expenses of $4.1 million, of which $2.2 million were paid in 2018. Upon the closing of the IPO, all shares of the Company's outstanding convertible preferred stock were automatically converted to 47,283,839 shares of common stock and the related carrying amount of $295.1 million was reclassified to common stock and additional paid-in capital within stockholders' equity (deficit).

Concurrent with the closing of the IPO, the Company also issued 4,121,683 shares of its common stock to Merck in a private placement at a price of $16.00 per share for proceeds of $65.9 million, which resulted in Merck owning approximately 19.9% of the Company's outstanding shares of common stock *(Note 6)*.

2. Summary of Significant Accounting Policies

Basis of Presentation and Principles of Consolidation

The accompanying consolidated financial statements have been prepared in accordance with U.S. GAAP and include the consolidated accounts of the Company and its subsidiary. These consolidated financial statements include the consolidated accounts of the Company and its wholly-owned foreign subsidiary in Australia. All intercompany balances and transactions have been eliminated upon consolidation.

Use of Estimates

The preparation of consolidated financial statements in conformity with U.S. GAAP requires management to make judgments, assumptions and estimates that affect the reported amounts of assets, liabilities, revenues and expenses. Specific accounts that require management estimates include, but are not limited to, stock-based compensation, the valuation of convertible preferred stock warrants, the fair value of convertible preferred and common stock, contract manufacturing and clinical trial accruals, collaboration revenue and associated

transaction price determined in accordance with Accounting Standards Codification Topic 606, Revenue from Contracts with Customers ("ASC 606"). Management bases its estimates on historical experience and on various other assumptions that are believed to be 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 could differ materially from those estimates.

Need for Additional Capital

Since inception, the Company has incurred net losses and negative cash flow from operations. During the years ended December 31, 2019, 2018 and 2017, the Company incurred net losses of $42.8 million, $0.5 million and $14.2 million, respectively. As of December 31, 2019, the Company had an accumulated deficit of $196.1 million and does not expect to experience positive cash flows from operations in the near future. The Company had $344.5 million of cash, cash equivalents and marketable securities as of December 31, 2019, and therefore the Company expects that its cash and cash equivalents and marketable securities will be sufficient to fund its operations for a period of at least one year from the date these consolidated financial statements are available for issuance. To fully implement the Company's business plan and fund its operations, the Company will need to raise additional capital through the issuance of equity securities or debt financings, collaborations, strategic alliances and licensing arrangements, government or other third-party funding or a combination of these.

Deferred Initial Public Offering Costs

Costs incurred in connection with the IPO primarily consisted of direct incremental legal, printing and accounting fees. IPO costs were capitalized as incurred and upon completion of the IPO, these costs were offset against the proceeds and recorded in additional paid-in capital. As of December 31, 2019 and 2018, deferred IPO costs included on the accompanying consolidated balance sheets were zero and $2.3 million, respectively.

Fair Value of Financial Instruments

The carrying amounts of cash and cash equivalents, the related party receivables from collaboration and other current assets and liabilities approximate their respective fair values because of the short-term nature of those instruments. Fair value accounting is applied to the convertible preferred stock warrant liabilities that were recorded at their estimated fair value in the consolidated financial statements.

Cash and Cash Equivalents

Cash and cash equivalents are stated at fair value. Cash equivalents are securities with an original maturity of three months or less at the time of purchase. The Company limits its credit risk associated with cash and cash equivalents by placing its investments with a bank it believes is highly creditworthy and with highly rated money market funds. As of December 31, 2019 and 2018, cash and cash equivalents consisted of bank deposits and investments in money market funds.

Marketable Securities

The appropriate classification of the Company's marketable securities is determined at the time of purchase and such designations are re-evaluated at each balance sheet date. All of the Company's securities are considered as available-for-sale and carried at estimated fair values and reported in cash equivalents, short-term marketable securities or long-term marketable securities. Unrealized gains and losses on available-for-sale securities are excluded from net loss and reported in accumulated other comprehensive loss as a separate component of stockholders' equity (deficit). Other income (expense), net, includes interest, amortization of purchase premiums and accretion of purchase discounts, realized gains and losses on sales of securities and other-than-temporary declines in the fair value of securities, if any. The cost of securities sold is based on the specific identification method.

The Company's investments are regularly reviewed for other-than-temporary declines in fair value. This review includes the consideration of the cause of the impairment, including the creditworthiness of the security issuers, the number of securities in an unrealized loss position, the severity and duration of the unrealized losses, whether the Company has the intent to sell the securities and whether it is more likely than not that the Company will be required to sell the securities before the recovery of their amortized cost basis. When the Company determines that the decline in fair value of an investment is below its carrying value and this decline is other-than-temporary, the Company reduces the carrying value of the security it holds and records a loss for the amount of such decline.

Restricted Cash

The Company's restricted cash represents collateral in connection with the lease on the Company's headquarters entered into in 2015 and is classified as a non-current asset on the consolidated balance sheets as the collateral will not be returned to the Company in less than 12 months *(Note 7)*.

Concentration of Credit and Other Risks

Cash and cash equivalents and marketable securities from the Company's available-for-sale and marketable security portfolio potentially subject the Company to concentrations of credit risk. The Company is invested in money market funds and marketable securities through custodial relationships with major U.S. and Australian banks. Under its investment policy, the Company limits amounts invested in such securities by credit rating, maturity, industry group, investment type and issuer, except for securities issued by the U.S. government.

Related party receivables from collaborations *(Notes 5 and 6)* are typically unsecured. Accordingly, the Company may be exposed to credit risk generally associated with its current Collaboration Agreement with Merck and any future collaboration agreements with other collaboration partners. To date, the Company has not experienced any losses related to these receivables.

Merck accounted for 100% of the Company's revenue for the years ended December 31, 2019, 2018 and 2017.

Property and Equipment, Net

Property and equipment is recorded at cost and consists of computer equipment, laboratory equipment and office furniture and leasehold improvements. Maintenance and repairs, and training on the use of equipment, are expensed as incurred. Costs that improve assets or extend their economic lives are capitalized. Depreciation is recognized using the straight-line method based on an estimated useful life of the asset, which is as follows:

Computer equipment	3 years
Laboratory equipment and office furniture	3 years
Leasehold improvement	Shorter of life of asset or lease term

Leases

The Company's lease agreements for its laboratory and office facilities are classified as operating leases. Rent expense is recognized on a straight-line basis over the term of the lease. Incentives granted under the Company's facilities leases, including allowances to fund leasehold improvements and rent holidays, are capitalized and are recognized as reductions to rental expense on a straight-line basis over the term of the lease.

Impairment of Long-Lived Assets

Long-lived assets, such as property and equipment, are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability of assets to be held and used is measured by a comparison of the carrying amount of an asset to the estimated undiscounted future cash flows expected to be generated by the asset. If the carrying amount of an asset exceeds its estimated undiscounted future cash flows, an impairment charge is recognized as the amount by which the carrying amount of the asset exceeds the estimated fair value of the asset. As of December 31, 2019 and 2018, no revision to the remaining useful lives or write-down of long-lived assets was required.

Income Taxes

Income taxes are accounted for under the liability method. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to the differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and the operating loss and tax credit carryforwards. Valuation allowances are established when necessary to reduce deferred tax assets to the amount expected to be realized. Deferred tax assets and liabilities are measured at the balance sheet date using the enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in the period such tax rate changes are enacted.

Convertible Preferred Stock Warrant

Freestanding warrants to purchase the Company's convertible preferred stock were classified as a liability on the consolidated balance sheet at December 31, 2018 as the underlying shares of convertible preferred stock were contingently redeemable, which could have obligated the Company to transfer assets at some point in the future to settle the warrants. The convertible preferred stock warrants are subject to remeasurement at each balance sheet date, with changes in estimated fair value recorded in the Company's consolidated statements of operations as a component of total other income (expense), net. On February 3, 2019, all convertible preferred stock warrants were automatically exercised on a net basis into 16,380 shares of Series A convertible preferred stock at a fair value of $0.2 million. As of December 31, 2019, there were no convertible preferred stock warrants outstanding.

Revenue Recognition

On January 1, 2019, the Company adopted ASU 2014-09, Revenue from Contracts with Customers (Topic 606), and subsequent amendments, using the modified retrospective transition method applied to those contracts that were not completed as of January 1, 2019. ASC 606 supersedes all prior revenue recognition guidance. Results for operating periods beginning after January 1, 2019 are presented under ASC 606, while prior period amounts have not been adjusted and continue to be reported in accordance with previous accounting rules under Accounting Standards Codification Topic 605, Revenue Recognition ("ASC 605").

Prior to the adoption of ASC 606, the Company's revenue from collaboration agreements was recognized when the Company determined that persuasive evidence of an arrangement exists, services had been rendered, the price was fixed or determinable and collectability was reasonably assured. The Company would record amounts received prior to satisfying the above revenue recognition criteria as deferred revenue until all applicable revenue recognition criteria were met. Revenue allocated to research activities was generally recognized in the period the services were performed, and revenue allocated to licenses was generally recognized on a straight-line basis over the contractual term. Allocations to non-contingent elements were based on the relative selling price of each element using vendor-specific objective evidence or third-party evidence, where available. In the absence of either of these measures, the Company used the best estimate of selling price for that deliverable.

The most significant change to the Company's policies upon the adoption of ASC 606 is the estimation of an arrangement's total transaction price, which includes unconstrained variable consideration, and the recognition of that transaction price based on a cost-based input method that requires estimates to determine, at each reporting period, the percentage of completion based on the estimated total effort required to complete the project and the total transaction price. Given the differences in revenue recognition policies, the revenue recognized in prior years is not strictly comparable to revenue recorded in the year ending December 31, 2019 or in future periods (see *Note 2 – Recently Adopted Accounting Pronouncements*).

The core principle in ASC 606 requires an entity to recognize revenue upon the transfer of goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. The Company applies the following five-step revenue recognition model outlined in ASC 606 to adhere to this core principle: (1) identify the contract(s) with a customer; (2) identify the performance obligations in the contract; (3) determine the transaction price; (4) allocate the transaction price to the performance obligations in the contract; and (5) recognize revenue when (or as) the Company satisfies a performance obligation.

All of the Company's revenue to date has been generated from its collaboration agreements. The terms of these agreements generally require the Company to provide (i) license options for its compounds, (ii) research and development services and (iii) non-mandatory services in connection with participation in research or steering committees. Payments received under these arrangements may include non-refundable upfront license fees, partial or complete reimbursement of research and development costs, contingent consideration payments based on the achievement of defined collaboration objectives and royalties on sales of commercialized products. In some agreements, the collaboration partner is solely responsible for meeting defined objectives that trigger contingent or royalty payments. Often the partner only pursues such objectives subsequent to exercising an optional license on compounds identified as a result of the research and development services performed under the collaboration agreement.

The Company assesses whether the promises in its arrangements, including any options provided to the customer, are considered distinct performance obligations that should be accounted for separately. Judgment is required to determine whether the license to a compound is distinct from research and development services or participation in steering committees, as well as whether options create material rights in the contract.

The transaction price in each arrangement is generally comprised of a non-refundable upfront fee and unconstrained variable consideration related to the performance of research and development services. The Company typically submits a budget for the research and development services to the customer in advance of performing the services. The transaction price is allocated to the identified performance obligations based on the standalone selling prices ("SSP") of each distinct performance obligation. Judgment is required to determine SSP. In instances where SSP is not directly observable, such as when a license or service is not sold separately, SSP is determined using information that may include market conditions and other observable inputs. The Company utilizes judgment to assess the nature of its performance obligations to determine whether they are satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress toward completion. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

The Company's collaboration agreements may include contingent payments related to specified development and regulatory milestones or contingent payments for royalties based on sales of a commercialized product. Milestones can be achieved for such activities in connection with progress in clinical trials, regulatory filings in various geographical markets and marketing approvals from regulatory authorities. Sales-based royalties are generally related to the volume of annual sales of a commercialized product. At the inception of each agreement that includes such payments, the Company evaluates whether the milestones are considered probable of being achieved and estimates the amount to be included in the transaction price by using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the Company's or its customer's control, such as those related to regulatory approvals, are not considered probable of being achieved until those approvals are received. The transaction price is then allocated to each performance obligation based on a relative SSP basis. At the end of each subsequent reporting period, the Company re-evaluates the probability of achievement of each such milestone and any related constraint and, if necessary, adjusts its estimate of the overall transaction price. Pursuant to the guidance in ASC 606, sales-based royalties are not included in the transaction price. Instead, royalties are recognized at the later of when the performance obligation is satisfied or partially satisfied, or when the sale that gives rise to the royalty occurs.

Research and Development

Research and development costs are expensed as incurred. Research and development expenses primarily include salaries and benefits for medical, clinical, quality, preclinical, manufacturing and research personnel, costs related to research activities, preclinical studies, clinical trials, drug manufacturing expenses and allocated overhead and facility occupancy costs. The Company accounts for non-refundable advance payments for goods or services that will be used in future research and development activities as expenses when the goods have been received or when the service has been performed rather than when the payment is made.

Clinical trial costs are a component of research and development expenses. The Company expenses costs for its clinical trial activities performed by third parties, including CROs and other service providers, as they are incurred, based upon estimates of the work completed over the life of the individual study in accordance with associated agreements. The Company uses information it receives from internal personnel and outside service providers to estimate the clinical trial costs incurred.

Stock-Based Compensation

The Company's stock-based compensation programs include stock options and shares that will be issued under the Company's 2019 ESPP. Stock-based compensation to employees is valued on the grant date of each award using the Black-Scholes option-pricing model, and its estimated fair value is recognized over the period during which the employee is required to provide service in exchange for the award, which is generally the vesting period of each award. Subsequent to the adoption of ASU 2018-07, Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting on January 1, 2019, stock-based compensation expense for non-employee stock-based awards is also measured based on the fair value on grant date with its estimated fair value recorded over the period for which the non-employee is required to provide service in exchange for the award. As non-cash stock-based compensation expense is based on awards ultimately expected to vest, it is

reduced by an estimate for future forfeitures. Forfeitures are estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures materially differ from estimates.

Foreign Currency Transactions

The functional currency of NGM Biopharmaceuticals Australia Pty Ltd., a wholly-owned subsidiary, is the U.S. Dollar. Accordingly, all monetary assets and liabilities of the subsidiary are remeasured into U.S. Dollars at the current period-end exchange rates and non-monetary assets are remeasured using historical exchange rates. Income and expense elements are remeasured to U.S. Dollars using the average exchange rates in effect during the period. Remeasurement gains and losses are recorded as other income (expense), net on the consolidated statements of operations.

The Company is subject to foreign currency risk with respect to its clinical and manufacturing contracts denominated in currencies other than the U.S. Dollar, primarily British Pounds, Swiss Francs, Australian Dollars and the Euro. Payments on contracts denominated in foreign currencies are made at the spot rate on the day of payment. Changes in the exchange rate between billing dates and payment dates are recorded within other income (expense), net on the consolidated statements of operations.

Comprehensive Loss

Comprehensive loss is comprised of net loss and certain changes in equity that are excluded from net loss. For the years ended December 31, 2019, 2018 and 2017, the difference between comprehensive loss and net loss consisted of changes in net unrealized gain on marketable securities of $0.3 million, net unrealized gain on marketable securities of $0.2 million and net unrealized loss on marketable securities of $0.3 million, respectively.

Net Loss per Share

Basic net loss per share is calculated by dividing net loss by the weighted average number of shares outstanding during the period, less shares subject to repurchase and excludes any dilutive effects of stock-based awards and warrants. Diluted net loss per share is computed giving effect to all potentially dilutive shares, including common stock issuable upon exercise of stock options, and unvested restricted common stock and stock units. As the Company had net losses for the years ended December 31, 2019, 2018 and 2017, all potential shares were determined to be anti-dilutive.

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

	Year Ended December 31,		
	2019	**2018**	**2017**
Numerator:			
Net loss	$ (42,795)	$ (493)	$ (14,159)
Denominator:			
Weighted average number of shares used in calculating net loss per share—basic and diluted	50,297,524	6,383,751	5,961,767
Net loss per share—basic and diluted	$ (0.85)	$ (0.08)	$ (2.37)

Potential gross dilutive securities that were not included in the diluted per share calculations because they would be anti-dilutive were as follows:

	Year Ended December 31,		
	2019	**2018**	**2017**
Convertible preferred stock	—	47,267,466	47,267,466
Options to purchase common stock	10,824,780	9,806,689	8,468,702
Warrants to purchase convertible preferred stock	—	19,637	19,637
Shares committed under ESPP	396,682	—	—
Total	11,221,462	57,093,792	55,755,805

Segment and Geographical Information

The Company operates in one segment. Substantially all of the Company's long-lived assets, primarily comprised of property and equipment, are based in the United States. For the years ended December 31, 2019, 2018 and 2017, the Company's revenues were entirely within the United States.

Recent Accounting Pronouncements

New accounting pronouncements are issued by the Financial Accounting Standards Board ("FASB") or other standard setting bodies and adopted by the Company as of the specified effective date. Unless otherwise discussed, the impact of recently issued standards that are not yet effective will not have a material impact on our consolidated financial statements upon adoption. Under the JOBS Act, the Company meets the definition of an emerging growth company, and has elected the extended transition period for complying with new or revised accounting standards pursuant to Section 107(b) of the JOBS Act.

Recently Adopted Accounting Pronouncements

In June 2018, the FASB issued ASU 2018-07, Compensation – Stock Compensation (Topic 718): Improvements to Non-Employee Share-Based Payment Accounting as part of the FASB simplification initiative. The new standard expands the scope of Topic 718, allowing the Company to apply the requirements of Topic 718 to certain non-employee awards issued in exchange for the acquisition of goods and services from non-employees. ASU 2018-07 is intended to supersede Subtopic 505-50, Equity-Based Payments to Non-Employees and is effective for the Company for fiscal years beginning after December 15, 2019. Effective January 1, 2019, the Company early adopted this ASU using the modified retrospective transition method in which all previously issued equity-classified share-based payment awards to non-employees were remeasured at fair value as of the adoption date. Newly issued equity-classified share-based payments awards to non-employees are measured at fair value as of grant date. The adoption of this ASU did not have a material impact on the Company's consolidated financial statements.

In May 2014, the FASB issued ASU 2014-09, Revenue from Contracts with Customers (Topic 606), which requires an entity to recognize the amount of revenue to which it expects to be entitled for the transfer of promised goods or services to customers. ASU 2014-09 replaced existing revenue recognition guidance and permits the use of either the full retrospective or modified retrospective transition method. Additionally, in March 2016, the FASB issued ASU 2016-08, Revenue from Contracts with Customers (Topic 606): Principal versus Agent Considerations (Reporting Revenue Gross versus Net), which clarifies the implementation guidance on principal versus agent considerations in ASU 2014-09. In April 2016, the FASB issued ASU 2016-10, Revenue from Contracts with Customers (Topic 606): Identifying Performance Obligations and Licensing, which clarifies certain aspects of identifying performance obligations and licensing implementation guidance. In May 2016, the FASB issued ASU 2016-12, Revenue from Contracts with Customers (Topic 606): Narrow-Scope Improvements and Practical Expedients, which relates to disclosures of remaining performance obligations, as well as other amendments to guidance on collectability, non-cash consideration and the presentation of sales and other similar taxes collected from customers. For the Company, these standards (collectively, ASC 606) have the same effective date and transition date of January 1, 2019.

The Company adopted ASC 606 on January 1, 2019, using the modified retrospective transition method and, therefore, evaluated its contract with Merck under ASC 606. The Company recorded adjustments upon the adoption of ASC 606 as a result of the Company concluding that licenses and research and development services promised in the agreement are a single combined performance obligation. This determination impacts the timing of recognition of both the non-refundable upfront fee and the payments related to the services. Under previous guidance, the upfront fee was recognized ratably over the contract term, and fees related to the services were recognized in the period the services were performed. Under ASC 606, revenue for the single performance obligation is recognized over time using a cost-based input method to measure progress toward completion of the single combined performance obligation.

The adoption of ASC 606 impacted the Company's contract liabilities and accumulated deficit balance as of January 1, 2019 as follows (in thousands):

	December 31, 2018	Adjustments due to the Adoption of ASC 606	January 1, 2019
Deferred revenue, current	$ 19,025	$ 5,171	$ 24,196
Deferred revenue, noncurrent	3,942	985	4,927
Accumulated deficit	(147,193)	(6,156)	(153,349)

The impact of the adoption of ASC 606 on the consolidated balance sheet as of December 31, 2019, consolidated statement of operations and cash flows for the year ended December 31, 2019 was as follows (in thousands):

	As of December 31, 2019		
	Amount Under ASC 605	Effect of Adoption Higher (Lower)	As Reported
Deferred revenue, current	$ 3,887	$ 985	$ 4,872
Accumulated deficit	(195,159)	(985)	(196,144)

	Year Ended December 31, 2019		
	Amount Under ASC 605	Effect of Adoption Higher (Lower)	As Reported
Related party revenue	$ 98,373	$ 5,171	$ 103,544
Loss from operations	(54,511)	5,171	(49,340)
Net loss	(47,966)	5,171	(42,795)
Net loss per common share, basic and diluted	(0.95)		(0.85)

	Year Ended December 31, 2019		
	Amount Under ASC 605	Effect of Adoption Higher (Lower)	As Reported
Cash flows from operating activities:			
Net loss	$ (47,966)	$ 5,171	$ (42,795)
Changes in operating assets and liabilities:			
Deferred revenue	(19,080)	(5,171)	(24,251)

Recent Accounting Pronouncements Not Yet Adopted

In February 2016, the FASB issued ASU 2016-02, Leases (Topic 842), which increases lease transparency and comparability among organizations. Under the new standard, lessees will be required to recognize right-of-use ("ROU") assets and lease liabilities arising from lease arrangements on the consolidated balance sheets, with the exception of leases with a term of 12 months or less, which permits a lessee to make an accounting policy election by class of underlying asset not to recognize the ROU assets and lease liabilities. In March 2018, the FASB approved an alternative transition method to the modified retrospective approach, which eliminates the requirement to restate prior period consolidated financial statements and allows the cumulative effect of the retrospective allocation to be recorded as an adjustment to the opening balance of retained earnings at the date of adoption. In November 2019, the FASB issued ASU 2019-10, which defers the effective date for certain ASUs including ASU 2016-02. The new guidance is now effective for the Company's fiscal year beginning after December 15, 2020, and interim periods within fiscal years beginning after December 15, 2021.

The Company plans to adopt the new lease standard using the optional transition method, which allows the Company to recognize a cumulative-effect adjustment to the opening balance of accumulated deficit at the date of adoption and apply the new disclosure requirements beginning in the period of adoption. The Company also plans to elect the package of practical expedients permitted under the transition guidance within the new standard, which, among other things, allows the Company to carryforward the historical lease classification and make an accounting policy election whereby ROU assets and lease liabilities associated with lease arrangements with terms less than one year will not be recognized. We will continue to evaluate the effect that this guidance will have on our consolidated financial statements.

In June 2016, the FASB issued ASU 2016-13, Financial Instruments – Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments. The new guidance amended guidance on reporting credit losses for assets held at amortized cost basis and available-for-sale debt securities. For available-for-sale debt securities, credit losses will be presented as an allowance rather than as a write-down. This standard is effective for the Company's fiscal year beginning after December 15, 2020. Early adoption is permitted for all entities. The Company is currently assessing the timing of adoption and the impact that the adoption of ASU 2016-13 will have on its consolidated financial statements.

In August 2018, the FASB issued ASU 2018-13, Fair Value Measurements (Topic 820): Disclosure Framework – Changes to the Disclosure Requirements for Fair Value Measurement as part of the FASB's disclosure framework project. This ASU modifies the disclosure requirements on fair value measurements in Topic 820, Fair Value Measurement by removing the requirement to disclose amounts of and reasons for transfers between Level 1 and Level 2 of the fair value hierarchy, the policy for timing of transfers between levels and the valuation process for Level 3 fair value measurements. This ASU also modifies existing disclosure requirements by clarifying that the measurement uncertainty disclosure is to communicate information about the uncertainty in measurement as of the reporting date, and it adds required disclosures for the changes in unrealized gains and losses for the period included in other comprehensive income for recurring Level 3 fair value measurements held at the end of the reporting period, and the range and weighted average of significant unobservable inputs used to develop Level 3 fair value measurements. This ASU will be effective for the Company for fiscal years and interim periods within those fiscal years, beginning after December 15, 2019. The Company is currently assessing the impact of this ASU on its consolidated financial statements.

In November 2018, the FASB issued ASU 2018-18, Collaborative Arrangements (ASC 808): Clarifying the Interaction between ASC 808 and ASC 606, which clarifies that certain transactions between collaborative arrangement participants should be accounted for as revenue under ASC 606 when the collaborative arrangement participant is a customer in the context of a unit of account. In those situations, all the guidance in ASC 606 should be applied, including recognition, measurement, presentation and disclosure requirements. This ASU adds unit-of-account guidance in ASC 808 to align with the guidance in ASC 606 (that is, a distinct good or service) when an entity is assessing whether the collaborative arrangement or a part of the arrangement is within the scope of ASC 606, and requires that in a transaction with a collaborative arrangement participant that is not directly related to sales to third parties, presenting the transaction together with revenue recognized under ASC 606 is precluded if the collaborative arrangement participant is not a customer. This ASU will be effective for the Company for fiscal years beginning after December 15, 2020, and interim periods within fiscal years beginning after December 15, 2021. The Company is currently assessing the impact of this ASU on its consolidated financial statements.

In December 2019, the FASB issued ASU 2019-12, Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes. The new guidance modifies ASC 740 to simplify several aspects of accounting for income taxes, including eliminating certain exceptions to the guidance in ASC 740 related to the approach for intraperiod tax allocation. This ASU will be effective for fiscal years after December 15, 2021, and interim periods within fiscal years beginning after December 15, 2022, and is required to be adopted prospectively, with the exception of certain specific amendments. The Company is currently assessing the impact of this ASU on its consolidated financial statements.

3. Fair Value Measurements

Financial assets and liabilities are recorded at fair value. The carrying amount of certain financial instruments, including cash and cash equivalents, receivable from collaboration, related party receivable from collaboration and other current assets and liabilities approximate fair value due to their relatively short maturities. Assets and liabilities recorded at fair value on a recurring basis in the balance sheets are categorized based upon the level of judgment associated with the inputs used to measure their fair values. Fair value accounting is applied to the convertible preferred stock warrant liabilities that are recorded at their estimated fair value in the consolidated financial statements.

The FASB has defined fair value as the exchange price that would be received for an asset or paid to transfer a liability, or an exit price, in the principal or most advantageous market for that asset or liability in an orderly transaction between market participants on the measurement date, and established a fair value hierarchy that requires an entity to maximize the use of observable inputs, where available, and minimize the use of unobservable inputs when measuring fair value. The FASB set forth three levels of inputs that may be used to measure fair value:

Level 1: Quoted prices in active markets for identical assets or liabilities.

Level 2: Observable inputs other than Level 1 prices, such as quoted prices for similar assets or liabilities, quoted prices in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

Level 3: Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

Assets and liabilities measured at fair value are classified in their entirety based on the lowest level of input that is significant to the fair value measurement. The Company's assessment of the significance of a particular input to the fair value measurement in its entirety requires management to make judgments and consider factors specific to the asset or liability.

To date, the Company has not recorded any impairment charges on marketable securities other than temporary declines in market value. In determining whether a decline is other than temporary, the Company considers various factors including the length of time and extent to which the market value has been less than cost, the financial condition and near-term prospects of the issuer and the Company's intent and ability to retain its investment in the issuer for a period of time sufficient to allow for any anticipated recovery in market value.

The Company estimates the fair values of investments in corporate agency bond securities, commercial paper and government agencies securities using level 2 inputs, by taking into consideration valuations obtained from third-party pricing services. The pricing services utilize industry standard valuation models, including both income and market-based approaches, for which all significant inputs are observable, either directly or indirectly, to estimate fair value. These inputs include reported trades of and broker/dealer quotes on the same or similar securities, issuer credit spreads, benchmark securities, prepayment/default projections based on historical data and other observable inputs.

Cash and cash equivalents and marketable securities, all of which are classified as available-for-sale securities consisted of the following (in thousands):

	Amortized Cost	Gross Unrealized Gain	Gross Unrealized Loss	Fair Value
As of December 31, 2019				
Money market funds	$ 244,973	$ —	$ —	$ 244,973
Corporate and agency bonds	66,063	14	—	66,077
Commercial paper	24,840	—	—	24,840
U.S. government agencies securities	7,985	11	—	7,996
Total	$ 343,861	$ 25	$ —	$ 343,886
Classified as:				
Cash and cash equivalents				$ 244,973
Short-term marketable securities (amortized cost of $98,888)				98,913
Total cash equivalents and marketable securities				$ 343,886

	Amortized Cost	Gross Unrealized Gain	Gross Unrealized Loss	Fair Value
As of December 31, 2018				
Money market funds	$ 34,983	$ —	$ —	$ 34,983
Corporate and agency bonds	68,322	—	(241)	68,081
Commercial paper	17,904	—	—	17,904
U.S. government agencies securities	63,751	—	(26)	63,725
Total	$ 184,960	$ —	$ (267)	$ 184,693
Classified as:				
Cash and cash equivalents				$ 34,983
Short-term marketable securities (amortized cost of $149,977)				149,710
Total cash equivalents and marketable securities				$ 184,693

Cash and cash equivalents in the table above excludes cash on deposit with banks of $0.6 million and $21.9 million as of December 31, 2019 and 2018, respectively.

As of December 31, 2019 and 2018, the Company's marketable securities all had remaining contractual maturities less than one year.

Assets and Liabilities Measured at Fair Value on a Recurring Basis

The following table sets forth the estimated fair value of the Company's financial assets and liabilities that were measured at fair value on a recurring basis as of December 31, 2019 and 2018 (in thousands):

	Fair Value Measurements			
As of December 31, 2019	**Level 1**	**Level 2**	**Level 3**	**Total**
Assets:				
Money market funds	$ 244,973	$ —	$ —	$ 244,973
Corporate and agency bonds	—	66,077	—	66,077
Commercial paper	—	24,840	—	24,840
U.S. government agencies securities	—	7,996	—	7,996
	$ 244,973	$ 98,913	$ —	$ 343,886

As of December 31, 2018	Fair Value Measurements			
	Level 1	Level 2	Level 3	Total
Assets:				
Money market funds	$ 34,983	$ —	$ —	$ 34,983
Corporate and agency bonds	—	68,081	—	68,081
Commercial paper	—	17,904	—	17,904
U.S. government agencies securities	—	63,725	—	63,725
	$ 34,983	$ 149,710	$ —	$ 184,693
Liabilities:				
Convertible preferred stock warrant liability	$ —	$ —	$ 198	$ 198
	$ —	$ —	$ 198	$ 198

There were no transfers of assets or liabilities between the fair value measurement levels during the years ended December 31, 2019 and 2018.

The following table provides a summary of changes in the fair value of the Company's convertible preferred stock warrant liability (in thousands):

Fair Value Using Level 3 Inputs	Amounts
Balance at December 31, 2017	$ 121
Change in fair value of warrant liability included in other income (expense), net	77
Balance at December 31, 2018	$ 198
Balance at December 31, 2018	$ 198
Net exercise of preferred stock warrant to Series A preferred stock	(198)
Balance at December 31, 2019	$ —

On February 3, 2019, all of the warrants were automatically exercised on a net basis into shares of Series A preferred stock. There were no convertible preferred stock warrants outstanding as of December 31, 2019.

4. Balance Sheet Components

Property and Equipment

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

	December 31,	
	2019	2018
Computer equipment	$ 1,201	$ 1,123
Laboratory equipment and office furniture	21,652	18,977
Leasehold improvements	25,880	25,314
Construction in process	498	679
Total property and equipment, gross	49,231	46,093
Less: accumulated depreciation and amortization	(29,756)	(22,200)
Total property and equipment, net	$ 19,475	$ 23,893

Depreciation expense for the years ended December 31, 2019, 2018 and 2017 was approximately $7.6 million, $7.2 million and $6.4 million, respectively.

Accrued Liabilities

Accrued liabilities consist of the following (in thousands):

	December 31,	
	2019	2018
Accrued expenses	$ 2,901	$ 2,595
Clinical trials and research and development costs	11,051	4,844
Personnel-related costs	6,446	4,148
Manufacturing costs	2,593	2,416
Total accrued liabilities	$ 22,991	$ 14,003

5. Research Collaboration and License Agreements

Merck

In February 2015, the Company entered into the Collaboration Agreement with Merck, covering the discovery, development and commercialization of novel therapies across a range of therapeutic areas. Pursuant to this agreement, the Company received an upfront payment of $94.0 million in April 2015. Concurrent with entry into the Collaboration Agreement, the parties entered into a Stock Purchase Agreement in which Merck agreed to purchase 8,833,333 shares of Series E convertible preferred stock at a price of $12.00 per share, resulting in net proceeds of approximately $106.0 million. The Company considered the ASC 606 criteria for combining contracts and determined that the Collaboration Agreement and Stock Purchase Agreement should be combined into a single contract. The Company accounted for the overall agreement based on the fair values of the assets and services exchanged, resulting in $106.0 million allocated to the equity component and $94.0 million allocated to the revenue components.

The Collaboration Agreement became effective in March 2015 and has a non-cancellable five-year term running through March 16, 2020. The agreement included an exclusive worldwide license to our GDF15 receptor agonist program. In March 2019, Merck exercised its option to extend the research phase of the collaboration through March 16, 2022. Merck terminated its license to the GDF15 receptor agonist program effective May 31, 2019. The collaboration also includes a broad, multiyear drug discovery and early development program financially supported by Merck but scientifically directed by the Company with input from Merck. The Company determines the scientific direction and areas of therapeutic interest, with input from Merck, and is primarily responsible for the conduct of all research, preclinical and early clinical development activities, through human proof of concept. The Company makes the final determinations as to which compounds to advance into and through initial clinical trials, which to progress into human proof-of-concept studies and the design of any such studies, with input from Merck through various governance committees. The Company may terminate its participation in any of the governance committees by providing written notice to Merck of its intention to disband and no longer participate. Merck will fund both the internal and external costs of the Company's research and early development activities up to $75.0 million each year of the initial five-year term and during the extended two-year research period.

Upon completion of a human proof-of-concept study for a particular compound, regardless of the results of such study, Merck has the one-time option, at a cost of $20.0 million, to obtain an exclusive, worldwide license, on specified terms, to that compound, as well as to other molecules that are directed against the same target in the same manner. If Merck exercises its option, Merck will be responsible, at its own cost, for any further development and commercialization activities for compounds within that Optioned Program. Upon such exercise by Merck, the Company in turn has the right, at the start of the first Phase 3 clinical study for that compound, to elect to participate in a worldwide cost and profit share with Merck, as well as the option to co-detail the compound in the United States, or the Company can elect instead to receive milestones and royalties from Merck based on Merck's further development and commercialization of the compound. If the Company elects to participate in the cost and profit share, subject to certain limitations, Merck will provide the Company with financial assistance in the form of interest bearing advances of the Company's share of the overall development costs, which Merck will recoup from the Company's share of any profit ultimately resulting from sales of the compound and other compounds that reach commercialization. If the Company does not opt in to the cost and profit sharing option, then the Company is eligible to receive development and regulatory milestone payments upon the achievement of specific clinical development or regulatory events with respect to the licensed compound indications in the United States, EU and Japan of up to an aggregate of $449.0 million. The Company may also receive commercial

milestone payments up to $125.0 million and royalty payments of varying percentages based on the achievement of certain levels of net sales.

Under the Collaboration Agreement, the Company also granted Merck a worldwide, exclusive right to conduct research and development on small molecule compounds generated by Merck that have specified activity against any target that the Company is researching or developing under the research phase and about which the Company has generated unique biological insights. If Merck ultimately does not exercise its license option to the compound the Company has taken through a human proof-of-concept study that is directed to any such target, Merck's research license for its own small molecule program will become non-exclusive, but it will retain an exclusive license to any small molecule compounds that it has, as of that time, identified and developed. Merck has sole responsibility for the research and development of any of these small molecule compounds, at its own cost. The Company is eligible to receive milestone and royalty payments on small molecule compounds that are developed by Merck under the Company's license, in some cases at the same rates as those the Company is eligible to receive from Merck for a licensed program originating from the Company's own research and development efforts, provided that, but for use of the Company's proprietary information, Merck would not have discovered such small molecule compounds. However, the Company will not have the option to cost and profit share or the option to co-detail those small molecule products.

The research and early development program had an initial term of five years, until March 16, 2020. In March 2019, Merck exercised its option to extend the research phase of the collaboration through March 16, 2022. In connection with this extension, Merck agreed to continue to fund the Company's research and development efforts during the two-year extension period at the same levels as during the initial term and, in lieu of a $20.0 million extension fee that would have otherwise been payable to the Company, Merck will make additional payments totaling up to $20.0 million in support of the Company's research and development program activities across 2021 and the first quarter of 2022. Under the terms of the agreement, Merck is required to pay a $20.0 million extension fee if it elects to exercise its second option to extend the research phase of the collaboration through March 16, 2024.

At the end of the research phase, Merck has the right to either require the Company to continue to conduct research and development activities with respect to certain of the then-existing programs for up to three years, which we call the tail period, by agreeing to pay all its internal and external costs for related work, or to take over such selected programs and conduct such research and development activities itself, at its own cost.

The Company evaluated the Collaboration Agreement with Merck under ASC 606. The Company identified the following promised goods or services at the inception of the Collaboration Arrangement: (i) license to GDF15 receptor agonist program; (ii) license to pursue research and development and commercialization of small molecule compounds; (iii) performance of research and development services for five years; (iv) two options to extend performance of the research and development services, each for two additional years; and (v) options to obtain licenses to additional compounds after proof of concept trials. The Company determined the GDF15 receptor agonist program license and small molecule program license are not distinct from the research and development services, resulting in these items being combined into a single performance obligation.

The Company considered whether the options created material rights in the contract and concluded that the fee attached to the exercise of such options approximated the SSP of the promised goods or services included in the options. Therefore, the options do not give rise to material rights, are not performance obligations in the Collaboration Agreement and, if and when exercised, will be accounted for as separate arrangements under ASC 606.

The transaction price consists of the $94.0 million upfront fee and the potential funding amounts of up to $75.0 million per year for each of the first five years of the Collaboration Agreement. No milestones or other forms of consideration are included in the transaction price as those amounts are contingent upon Merck exercising an option for licenses on additional compounds and would, therefore, be pursuant to separate arrangements and are not part of the Collaboration Agreement estimated transaction price.

Additionally, if a separate arrangement is created by the exercise of an option, such amounts would then be contingent on events outside of either party's control, such as products proving to be commercially viable and governmental agencies granting regulatory approval. Such contingencies and uncertainties result in the amounts being constrained and withheld from inclusion in the estimated transaction price of a separate arrangement. Consequently, the estimated transaction price related to the Collaboration Agreement is comprised of the up-front payment and the ongoing research and development reimbursements.

Any fees associated with options, including upfront fees, funding fees, milestones, etc., are not included in the transaction price as they are associated with options that are not material rights and, thus, are not performance obligations within the Collaboration Agreement. This includes the $20.0 million license fee associated with Merck's exercise of its option on NGM313. That amount was recognized in the period of exercise (i.e., fourth quarter of 2018) as the Company has no further obligations related to that license. Merck exercised its option on the NGM313 compound and paid the Company the $20.0 million option exercise fee in November 2018. The Phase 3 clinical study for NGM313 has not begun, and the Company has not made an election as to whether it will participate in the cost and profit share or receive milestone and royalty payments. The amounts do not impact the estimated transaction price associated with the single performance obligation identified in the Collaboration Agreement.

As there is only one performance obligation in the Collaboration Agreement, the transaction price was allocated entirely to that performance obligation. The Company uses a cost-based input method to measure proportional performance and calculate the corresponding amount of revenue to recognize. The Company believes this is the best measure of progress given that other measures do not reflect how the Company transfers its performance obligation to Merck. In applying the cost-based input measure of revenue recognition, the Company measures actual costs incurred relative to budgeted costs to fulfill the combined performance obligation. These costs consist of full-time equivalent hours plus allowable external (third-party) costs incurred. Revenue is recognized based on actual costs incurred as a percentage of total budgeted costs as the Company completes its performance obligation. The Company re-evaluates the estimate of expected costs to satisfy the performance obligation each reporting period and makes adjustments for any significant changes.

On May 31, 2019, Merck terminated its license to the GDF15 receptor agonist program. The research and development services within the Collaboration Agreement are not affected by the GDF15 receptor agonist program license termination and are expected to continue through the remainder of the research program term.

As of December 31, 2019 and 2018, deferred revenue related to the single performance obligation in the Collaboration Agreement was $4.9 million and $23.0 million, respectively. Of the amount recognized for the adoption of ASC 606 in the reporting period ended December 31, 2019, $6.2 million was in deferred revenue at the end of the prior reporting period. As of December 31, 2018, $3.7 million was due from Merck under the Collaboration Agreement. To date, the Company has recognized revenue of approximately $367.8 million related to the single performance obligation in the Collaboration Agreement.

In connection with the Series E convertible preferred stock purchase agreement, the Company and Merck entered into an agreement whereby Merck agreed to purchase 4,121,683 shares of our common stock in a separate private placement concurrent with the completion of the Company's IPO at a price per share equal to the public offering price of $16.00, resulting in Merck owning approximately 19.9% of the Company's outstanding shares of common stock following the completion of the IPO.

The Company is also eligible to receive additional payments specific to Merck opting into an Optioned Program. Each Optioned Program is eligible to receive a one-time payment of $20.0 million upon Merck's exercise of its one-time option to obtain an exclusive, worldwide license to a compound following its completion of a human proof-of-concept study. In addition, if the Company does not opt into the cost and profit sharing option, then the Company is eligible to receive an aggregate of $449.0 million in milestone payments, of which $77.7 million relates to the potential achievement of specific clinical development events and $371.3 million relates to the potential achievement of certain regulatory events with respect to the licensed compounds for the first three indications in the United States, EU and Japan.

A breakout of the milestone payments in connection with the potential achievement of certain clinical development events is as follows (in thousands):

	First Indication	Second Indication	Third Indication
Upon administration of an applicable product to the first patient in the first Phase 3 clinical trial for such product for the given indication	$ 35,000	$ 25,250	$ 17,500

A breakout of the milestone payments in connection with the potential achievement of various regulatory events for each of the three indications, for each of the three geographic areas, is as follows (in thousands):

	First Indication	Second Indication	Third Indication	Total
United States	$ 75,000	$ 56,250	$ 37,500	$ 168,750
European Union	60,000	45,000	30,000	135,000
Japan	30,000	22,500	15,000	67,500
	$ 165,000	$ 123,750	$ 82,500	$ 371,250

Summary of Collaboration Revenue

The Company recognized revenue from its collaboration and license agreements as follows (in thousands):

	Year Ended December 31,		
	2019	2018	2017
Related party revenue	$ 103,544	$ 108,665	$ 77,141

For the year ended December 31, 2019, the Company recognized collaboration and license revenue under the Collaboration Agreement of $103.5 million, of which $24.0 million was recognized from the upfront license fee by applying the cost-based input measure of revenue recognition in accordance with ASC 606 and the remaining balance related to research and development activities. The Company also recognized collaboration and license revenue under the Collaboration Agreement of $108.7 million and $77.1 million for the years ended December 31, 2018 and 2017, which were comprised of $18.8 million of amortized upfront payments for each fiscal year, $20.0 million related to the licensing of NGM313 in 2018 and the remaining balance for each fiscal year related to research and develop activities reimbursed by Merck provided under the Collaboration Agreement.

The Company is also eligible to receive commercial milestone payments of up to $125.0 million payable for each licensed product. In addition, the Company is eligible to receive royalties at ascending low-double digit to mid-teen percentage rates, depending on the level of net sales Merck achieves worldwide for each licensed compound.

Contract Assets and Liabilities

Changes in contract liabilities under ASC 606 were as follows (in thousands):

	Amounts
Balance at December 31, 2018	$ 22,967
Adoption of ASC 606	6,156
Balance at January 1, 2019	29,123
Revenue recognized included in the contract liability balance at the beginning of the period	(24,251)
Balance at December 31, 2019	$ 4,872

There were no contract assets for all the periods presented.

6. Related Party Transactions

Revenues from related parties refer to the Collaboration Agreement with Merck. For the years ended December 31, 2019, 2018 and 2017, the Company recognized related party revenues of $103.5 million, $108.7 million and $77.1 million, respectively. As of December 31, 2019 and 2018, the Company had deferred revenue from the Collaboration Agreement of $4.9 million and $23.0 million, respectively.

Other related party transactions include the Company's assignment of its operating lease of 630 Gateway to Merck *(Note 7)* and the Company's private placement with Merck that occurred concurrently with the Company's IPO *(Note 1)*.

7. Commitments and Contingencies

Operating Lease and Lease Guarantee

In September 2009, the Company entered into an operating lease for a corporate office space and laboratory facility at 630 Gateway Blvd, in South San Francisco, California ("630 Gateway") for approximately 50,000 square feet, as amended in June 2014 ("2014 Lease Amendment"), which expires in November 2020. The 2014 Lease Amendment provided for tenant improvement allowances of $0.8 million. The 2014 Lease Amendment contains scheduled rent increases over the lease term and has an option for the Company to extend the lease for an additional three-year term.

In December 2015, the Company entered into a new operating lease for its corporate office space and laboratory facility at 333 Oyster Point Blvd, South San Francisco, California ("333 Oyster Point") for approximately 122,000 square feet that expires in December 2023. The lease provided a tenant improvement allowance of $15.2 million that the Company used in 2016 towards $22.3 million in total leasehold improvements that are amortized over the lease term of seven years.

The 333 Oyster Point lease agreement required a letter of credit in the amount of $2.3 million as a security deposit to the lease, which the Company has recorded as non-current restricted cash on the consolidated balance sheets. The Company has the right to reduce the letter of credit amount by $0.4 million on each of the third anniversary and fourth anniversary of the rent commencement date. For the year ended December 31, 2019, the Company reduced its letter of credit by $0.4 million and reclassified that amount from restricted cash to cash and cash equivalents on the consolidated balance sheets.

In July 2016, the Company assigned its operating lease of 630 Gateway to Merck, as part of the Company's relocation to 333 Oyster Point. As part of the assignment of the lease, the Company is liable to the lessor if Merck defaults on its lease obligations. Therefore, in substance, the Company has guaranteed the lease payments for 630 Gateway, including lease-related expenses such as utilities, property tax and common area maintenance without any limitations. The Company assessed the need for a potential guarantee liability on the assigned lease, and concluded that the value of the guarantee was insignificant as of December 31, 2019 due to the short duration of the remaining lease term through November 2020, and Merck's credit rating of AA/A1 and subsequent investment in tenant improvements to the facility. As of December 31, 2019 and 2018, the remaining lease payment obligations that are due for 630 Gateway were approximately $2.0 million and $3.9 million, respectively, which are to be paid directly from Merck to the lessor.

The Company recognizes rent expense on a straight-line basis over the lease period with the difference recorded as deferred rent. In addition, tenant improvement allowances recorded are amortized as a reduction to rent expense on a straight-line basis over the lease term. Rent expense under these facility operating leases was approximately $2.2 million for the years ended December 31, 2019, 2018 and 2017, respectively.

Future minimum payments under the unassigned lease obligations described above are as follows as of December 31, 2019 (in thousands):

Year Ended December 31,	
2020	$ 4,995
2021	5,141
2022	5,294
2023	5,455
Total	$ 20,885

Indemnification

In the normal course of business, the Company enters into contracts and agreements that contain a variety of representations and warranties and may provide for indemnification of the counterparty. The Company's exposure under these agreements is unknown because it involves claims that may be made against it in the future, but have not yet been made.

In accordance with the Company's amended and restated certificate of incorporation and its amended and restated bylaws, the Company has indemnification obligations to its officers and directors, subject to some limits, with respect to their service in such capacities. The Company has also entered into indemnification agreements with its directors and certain of its officers. To date, the Company has not been subject to any claims, and it maintains director and officer insurance that may enable it to recover a portion of any amounts paid for future potential claims.

The Company's exposure under these agreements is unknown because it involves claims that may be made against it in the future, but have not yet been made. The Company believes that the fair value of these indemnification obligations is minimal and, accordingly, it has not recognized any liabilities relating to these obligations for any period presented.

8. Convertible Preferred Stock

Upon the closing of the Company's IPO, each then outstanding share of convertible preferred stock was converted into shares of common stock. With respect to the Company's convertible preferred stock outstanding prior to the IPO, the Company elected to follow the SEC staff's guidance (included in ASC 480-10-S99, SEC Materials) when evaluating the classification of its shares within the consolidated balance sheets. A liquidation, winding up, change in control, or sale of substantially all assets of the Company could constitute a redemption event. Although the majority of the Company's preferred stock was not mandatorily or currently redeemable, a liquidation or winding up of the Company could have constituted an event outside its control. Therefore, all shares of convertible preferred stock have been presented outside the permanent equity for all periods presented due to its contingently redeemable nature.

Convertible preferred stock as of December 31, 2018, on an as-converted basis, consisted of the following (in thousands):

	Shares		Issuance Price per Share	Aggregate Liquidation Value	Aggregate Carrying Value
	Authorized	**Outstanding**			
Series A	13,295	13,275	$ 2.00	$ 26,550	$ 26,462
Series B	11,078	11,078	5.00	55,389	55,148
Series C	8,328	8,328	6.00	49,970	49,887
Series D	6,600	5,753	10.00	57,530	57,461
Series E	8,833	8,833	12.00	88,335	105,916
	48,134	47,267		$ 277,774	$ 294,874

In March 2015, the Company amended and restated its certificate of incorporation in conjunction with the Series E convertible preferred stock offering. Prior to the conversion of the convertible preferred stock upon closing of the IPO, the significant rights and obligations of the Company's convertible preferred stock were as follows:

Voting Rights: Each holder of convertible preferred stock was entitled to the number of votes equal to the number of shares of common stock into which such shares of convertible preferred stock were convertible. In the event the preferred stockholders controlled a majority of the board of directors through direct representation on the board of directors or through other rights, the stockholders could approve redemption of the preferred stock.

Dividends: Each holder of convertible preferred stock was entitled to receive non-cumulative dividends at the rate of 8% per annum for each share of convertible preferred stock outstanding, when, as and if declared by the board of directors. These dividends were payable in preference to common stock dividends. The Company did not declare or pay any dividends.

Liquidation: In the event of any liquidation, dissolution or winding-up of the Company, each holder of convertible preferred stock was entitled to receive payment out of the assets of the Company legally available for distribution for each share of convertible preferred stock held by the holder of an amount per share of preferred stock equal to the original issue price plus all declared and unpaid dividends on the convertible preferred stock, with the exception that the holder of the Series E convertible preferred stock was only eligible to receive an amount equal to $10.00 per share plus all declared and unpaid dividends on the convertible preferred stock. In the event that the available funds and assets were insufficient for full payment to the holders of convertible preferred stock on a per-share basis as outlined above, the entire assets and funds of the Company legally available for distribution would have been distributed ratably among the holders of convertible preferred stock in proportion to the full amount to which they would otherwise have been respectively entitled. Upon completion of the distribution of assets as set forth above, all of the remaining assets, if any, would have been distributed ratably among the holders of common stock.

As of December 31, 2019, the Company does not have any convertible preferred stock issued or outstanding.

9. Stockholders' Equity (Deficit)

Preferred Stock

The Company has 10,000,000 shares of preferred stock authorized, which may be issued at the discretion of the Company's board of directors. The board of directors may issue shares of preferred stock in one or more series and to fix the number, rights, preferences, privileges and restrictions. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences and sinking fund terms. As of December 31, 2019, the Company does not have any shares of preferred stock issued or outstanding.

Common Stock

As of December 31, 2019 and 2018, the Company had 66,960,279 and 6,937,890 shares of common stock outstanding, respectively, which included shares subject to repurchase of 74,454 and 205,108, respectively, as a result of early exercise of stock options not yet vested. As of December 31, 2019 and 2018, the Company reserved shares of common stock for issuance as follows:

	December 31,	
	2019	**2018**
Conversion of convertible preferred stock	—	47,267,466
Common stock options outstanding	10,824,780	9,806,689
Common stock options available for grant	5,316,066	2,125,875
Warrant to purchase convertible preferred stock	—	19,637
401(k) Matching Plan	28,274	36,751
ESPP shares available for purchase	897,255	—
Total	17,066,375	59,256,418

Stock Option Plan

In 2018, the Company adopted the 2018 Plan for eligible employees, officers, directors, advisors and consultants, which provides for the grant of incentive and non-statutory stock options, restricted stock awards and stock appreciation rights. The terms of the stock option agreements, including vesting requirements, are determined by the board of directors, subject to the provisions of the 2018 Plan. Options granted by the Company generally vest within four years and are exercisable from the grant date until ten years after the date of grant. Vesting of certain employee options may be accelerated in the event of a change in control of the Company. As of December 31, 2019, 17,874,624 shares of common stock had been authorized for issuance under the 2018 Plan. Pursuant to the terms of the 2018 Plan, the number of shares reserved and available to issue will automatically increase on January 1st of each year in an amount equal to 4% of the total number of common shares outstanding on the December 31st immediately preceding calendar year, unless the board of directors elects to forego or reduce such increase. The Company's 2008 Plan expired at the beginning of 2018.

Stock options are governed by stock option agreements between the Company and recipients of stock options. Prior to the closing of the Company's IPO, the board of directors exercised reasonable judgment and considered a number of objective and subjective factors to determine the best estimate of the fair value of our common stock, including the Company's stage of development; progress of its research and development efforts; the rights, preferences and privileges of its convertible preferred stock relative to those of its common stock; equity market conditions affecting comparable companies; and the lack of marketability of our common stock. Subsequent to the IPO, the exercise price of each option shall not be less than 100% of the fair market value of the common stock subject to the option on the date the option is granted. A 10% or greater stockholder shall not be granted an incentive stock option unless the exercise price of such option is at least 110% of the fair value of the common stock on the date of grant and the option is not exercisable after the expiration of five years from the grant date. Options become exercisable and expire as determined by the Compensation Committee, provided that the term of incentive stock options may not exceed ten years from the date of grant for options granted to those other than 10% stockholders.

Stock Option Activity

A summary of the outstanding stock options is as follows:

		Outstanding Options			
	Options Available for Grant	Number of Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Life (in Years)	Aggregate Intrinsic Value (in Thousands)
Balances at December 31, 2018	2,125,875	9,806,689	$ 5.86	6.62	$ 105,226
Additional shares reserved	5,193,322				
Options granted	(2,424,198)	2,424,198	12.84		
Options exercised	—	(987,479)	3.65		
Options cancelled	418,628	(418,628)	8.60		
Options repurchased	2,439	—	7.69		
Balances at December 31, 2019	5,316,066	10,824,780	$ 7.52	6.29	$ 118,770
Vested and expected to vest at December 31, 2019		10,727,013	$ 7.48	6.26	$ 118,143
Outstanding and exercisable at December 31, 2019		10,824,780	$ 7.52	6.29	$ 118,770

The aggregate intrinsic values of options outstanding, exercisable, vested and expected to vest were calculated as the difference between the exercise price of the options and the estimated fair value of the Company's common stock, as determined by the board of directors.

The weighted average grant-date fair value of stock options granted during the years ended December 31, 2019, 2018 and 2017 was $8.00, $5.71 and $4.60 per share, respectively. The intrinsic value of stock options exercised was $10.2 million, $1.9 million and $0.5 million for the years ended December 31, 2019, 2018 and 2017, respectively. The total grant-date fair value of stock options that vested during the years ended December 31, 2019, 2018 and 2017 was $10.0 million, $7.5 million and $5.2 million, respectively. Due to the Company's net operating losses, the Company did not realize any tax benefits from stock-based payment arrangements for the year ended December 31, 2019, 2018 and 2017.

Early Exercise of Stock Options

The 2018 Plan allows for the granting of options that may be exercised before the options have vested. Shares issued as a result of early exercise that have not vested are subject to repurchase by the Company upon termination of the purchaser's employment or services, at the price paid by the purchaser, and are not deemed to be issued for accounting purposes until those related shares vest. The amounts received in exchange for these shares have been recorded as a liability on the consolidated balance sheets and will be reclassified into common stock and additional paid-in-capital as the shares vest. The Company's right to repurchase these shares generally lapses in equal installments over four years beginning from the original vesting commencement date.

As of December 31, 2019, there were 74,454 shares of common stock outstanding subject to the Company's right of repurchase at prices ranging from $7.64 to $8.14 per share. At December 31, 2018, there were 205,108 shares of common stock outstanding subject to the Company's right of repurchase at prices ranging from $4.00 to $8.14 per share. As of December 31, 2019 and 2018, the Company recorded $0.6 million and $1.6 million, respectively, as early exercise stock option liabilities associated with shares issued with repurchase rights.

Employee Stock-Based Compensation Expense

Employee and director stock-based compensation expense was calculated based on awards ultimately expected to vest and has been reduced for estimated forfeitures. The following table summarizes stock-based compensation expense related to stock-based payment awards to employees and directors for the years ended December 31, 2019, 2018 and 2017, which was allocated as follows (in thousands):

	Year Ended December 31,		
	2019	2018	2017
Research and development	$ 7,145	$ 5,232	$ 4,473
General and administrative	5,584	4,524	2,994
Total stock-based compensation expense	$ 12,729	$ 9,756	$ 7,467

Valuation Assumptions

The Company uses the Black-Scholes option-pricing model to estimate the fair value of stock options at the grant date. The Black-Scholes option-pricing model requires the Company to make certain estimates and assumptions, including assumptions related to the expected price volatility of the Company's stock, the period during which the options will be outstanding, the rate of return on risk-free investments and the expected dividend yield for the Company's stock.

The fair value of stock option awards granted to employees and directors were estimated at the date of grant using a Black-Scholes option-pricing model with the following weighted average valuation assumptions:

	Year Ended December 31,		
	2019	2018	2017
Risk-free interest rate	2.25%	2.59%	1.73%
Expected term of options (in years)	6.18	5.98	6.25
Expected stock price volatility	64.85%	64.60%	75.48%
Forfeiture rate	2.20%	4.42%	3.04%
Expected dividends	—	—	—

The weighted average valuation assumptions were determined as follows:

Expected Stock Price Volatility: The expected volatility is based on the historical volatility of the stock of similar entities within the Company's industry over periods commensurate with the Company's expected term assumption.

Expected Term of Options: The expected term of options represents the period of time options are expected to be outstanding. The expected term of the options granted is derived using the "simplified" method (that is, estimating the expected term as the midpoint between the vesting date and the end of the contractual term for each option).

Risk-Free Interest Rate: The Company bases the risk-free interest rate on the interest rate payable on U.S. Treasury securities in effect at the time of grant for a period that is commensurate with the assumed expected option term.

Expected Annual Dividends: The Company has not historically paid, and does not expect for the foreseeable future to pay, a dividend.

Forfeiture Rate: The forfeiture rate represents the percentage of unvested stock options the Company expects will not vest, and, therefore, should not be expensed. The Company estimates forfeiture rates based on historical stock option grants and cancellations.

As of December 31, 2019, there was approximately $24.1 million in total unrecognized compensation expense, net of estimated forfeitures, related to unvested options granted to employees and directors under the 2008 and 2018 Plans. The expense is expected to be recognized over a weighted average period of 2.67 years.

Stock Options Granted to Non-employees

The Company grants stock options to non-employees in exchange for services performed for the Company. The Company granted 22,500 options to non-employees for the year ended December 31, 2019. For the years ended December 31, 2018 and 2017, the Company did not grant any options to non-employees. Stock-based compensation expense related to stock-based payment awards to non-employees for the years ended December 31, 2019, 2018 and 2017 was $133,000, $103,000 and $250,000, respectively. As of December 31, 2019 and December 31, 2018, non-employee stock options to purchase 21,564 and 16,042 shares, respectively, remained unvested.

The fair value of stock option awards granted to non-employees was estimated at the date of grant using a Black-Scholes option-pricing model with the following weighted average valuation assumptions:

	Year Ended December 31,		
	2019	**2018**	**2017**
Risk-free interest rate	2.26%	—	2.48%
Expected term of options (in years)	6.00	—	6.95
Expected stock price volatility	65.77%	—	64.93%
Expected dividends	—	—	—

2019 Employee Stock Purchase Plan

In March 2019, the Company adopted the 2019 ESPP. The Company reserved 1,000,000 shares of common stock pursuant to purchase rights granted to the Company's employees. The 2019 ESPP provides that the number of shares reserved and available for issuance will automatically increase on January 1 of each calendar year, beginning January 1, 2020, by the lesser of (1) 1.0% of the total number of shares of common stock outstanding on December 31 of the preceding calendar year, (2) 1,000,000 shares or (3) a number determined by our board of directors that is less than (1) and (2). The board of directors determined not to increase the number of shares reserved under the 2019 ESPP on January 1, 2020.

Under the 2019 ESPP, eligible employees are granted options to purchase shares of our common stock through payroll deductions that cannot exceed 15% of each employee's salary. The 2019 ESPP provides for a 24-month offering period, which includes four six-month purchase periods. At the end of each purchase period, eligible employees are permitted to purchase shares of common stock at the lower of 85% of fair market value at the beginning of the offering period or fair market value at the end of the purchase period. The 2019 ESPP is considered a compensatory plan and the Company has recorded stock-based compensation expense of $1.0 million for the year ended December 31, 2019. As of December 31, 2019, 102,745 shares of common stock were purchased under the 2019 ESPP.

The fair value of the rights granted to employees under the 2019 ESPP was estimated at the date of offer using a Black-Scholes option-pricing model with the following weighted average valuation assumptions:

	Year Ended December 31,		
	2019	2018	2017
Risk-free interest rate	1.97%	—	—
Expected term of options (in years)	1.23	—	—
Expected stock price volatility	59.46%	—	—
Expected dividends	—	—	—

10. Income Taxes

Income Taxes

For the years ended December 31, 2019 and 2018, there were no provision or benefit from income tax. The benefit from income taxes recognized for the year ended December 31, 2017 was $1.0 million, which was related to the Company's Minimum Tax Credit payments prior to enactment of the 2017 Tax Act. Of the benefit from income taxes recognized for the year ended December 31, 2017, the Company received $0.5 million in 2019.

The components of the Company's losses before income taxes were as follows (in thousands):

	Year Ended December 31,		
	2019	2018	2017
Domestic	$ (34,634)	$ 5,502	$ (8,974)
Foreign	(8,161)	(5,995)	(6,245)
Total	$ (42,795)	$ (493)	$ (15,219)

A reconciliation of the statutory U.S. federal rate to the Company's effective tax rate is as follows:

	Year Ended December 31,		
	2019	2018	2017
U.S. federal tax at statutory rate	21.0 %	21.0 %	34.0 %
Foreign Australian subsidiary	1.7	109.5	(1.6)
State, Net of Federal Benefit	0.0	(4.5)	1.3
Stock-based compensation	0.2	(93.1)	(14.5)
Change in valuation allowance	(23.2)	401.6	68.7
Tax reform tax rate change	—	—	(85.0)
Other	0.2	(434.7)	4.0
Total	0.0 %	(0.2) %	6.9 %

The components of the net deferred tax assets are as follows (in thousands):

	December 31,	
	2019	2018
Deferred tax assets:		
Net operating loss carryforwards	$ 37,679	$ 26,545
Stock-based compensation	3,478	1,961
Research and development credit	2,918	2,918
Deferred revenue	1,026	4,838
Other temporary differences	1,217	1,389
Total gross deferred tax assets	46,318	37,651
Deferred tax liabilities:		
Depreciation and amortization	(570)	(1,368)
Non-qualified stock options with 83(b) election	(15)	(54)
Total gross deferred tax liabilities	(585)	(1,422)
Net deferred tax assets before valuation allowance	45,733	36,229
Deferred tax asset valuation allowance	(45,733)	(36,229)
Net deferred tax assets	$ —	$ —

ASC 740 requires that the tax benefit of net operating losses, temporary differences and credit carryforwards be recorded as an asset to the extent that management assesses that realization is “more likely than not.” Realization of the future tax benefits is dependent on the Company’s ability to generate sufficient taxable income within the carryforward period. Because of the Company’s recent history of operating losses, management believes that recognition of the deferred tax assets arising from the above-mentioned future tax benefits is currently more-likely-than-not to be realized and, accordingly, has provided a valuation allowance.

Realization of deferred tax assets is dependent upon future earnings, if any, the timing and amount of which are uncertain. Accordingly, the net deferred tax assets have been fully offset by a valuation allowance. The valuation allowance increased by approximately $9.5 million and decreased by approximately $2.2 million during the years ended December 31, 2019 and 2018, respectively.

As of December 31, 2019, the Company had approximately $113.1 million in federal net operating loss carryforwards to reduce future taxable income. Of this amount, $47.7 million was generated after December 31, 2017 and do not expire as per the 2017 Tax Act and can be carried forward indefinitely. The federal net operating loss carryforwards generated prior to January 1, 2018 are subject to a 20-year carryforward period and will begin to expire after 2032. Subsequent to the enactment of the 2017 Tax Act, the utilization of the federal net operating loss carryforwards generated in fiscal year 2018 and onwards are limited to 80% of the federal taxable income. The Company also had approximately $71.9 million in state net operating loss carryforwards to reduce future taxable income which will begin to expire after 2028, if not utilized.

The Company had approximately $3.1 million and $3.1 million in federal research and development tax credits for the years ended December 31, 2019 and 2018, respectively. In addition, the Company had approximately $4.0 million and $4.0 million in state research and development tax credits for the years ended December 31, 2019 and 2018. The federal research credits will begin to expire in the years 2028 through 2035, if not utilized. The state research and development credits have no expiration date and can be carried forward indefinitely.

As of December 31, 2019 and 2018, the Company had foreign net operating loss carryforwards of approximately $29.7 million and $22.9 million, respectively, which have no expiration date.

Utilization of the Company’s net operating losses and credits may be subject to a substantial annual limitation due to the “change in ownership” provisions of the Internal Revenue Code of 1986, as amended, and similar state provisions. The annual limitation may result in the expiration of net operating losses and credits before utilization.

A reconciliation of the Company's unrecognized tax benefits for the years ended December 31, 2019, 2018 and 2017 is as follows (in thousands):

	December 31,		
	2019	2018	2017
Balance at beginning of year	$ 3,819	$ 1,528	$ 1,528
Additions (deletions) based on tax positions related to prior year	—	2,291	—
Balance at end of year	$ 3,819	$ 3,819	$ 1,528

There are approximately $3.8 million of unrecognized tax benefits included in the consolidated balance sheets that would, if recognized, affect the effective tax rate before consideration of valuation allowance. The Company does not believe that its unrecognized tax benefits will significantly change within the next 12 months.

It is the Company's practice to recognize interest and penalties related to income tax matters in income tax expense. As of December 31, 2019, the Company had no accrued interest and penalties related to uncertain tax positions.

The Company files federal, state, and foreign income tax returns with varying statutes of limitations. The tax years from inception in 2008 forward remain open to examination due to the carryover of unused net operating losses and tax credits.

11. Employee Benefit Plan

The Company sponsors a 401(k) defined contribution plan for its employees. Employee contributions are voluntary. In December 2011, the Company adopted the 401(k) Matching Plan, whereby the Company will make matching contributions in the form of common stock at a rate of $1.00 for each $2.00 of employee contributions up to a maximum $750 of common stock per year. As of December 31, 2019 and 2018, the Company had reserved 28,274 and 36,751 shares of common stock for issuance pursuant to the 401(k) Matching Plan, respectively. Matching contributions of 8,477 and 11,223 shares, or $106,000 and $103,000 were issued for the years ended December 31, 2019 and 2018, respectively.

12. Selected Quarterly Financial Data (Unaudited)

The following tables provide the selected quarterly financial data for the years ended December 31, 2019 and 2018 (in thousands, except share and per share amounts):

	2019			
	Q4	Q3	Q2	Q1
Related party revenue	$ 31,083	$ 21,568	$ 25,341	$ 25,552
Loss from operations	(17,294)	(12,997)	(9,707)	(9,342)
Net loss	(15,941)	(10,917)	(7,669)	(8,268)
Net loss per share, basic and diluted (2),(3)	$ (0.24)	$ (0.17)	$ (0.13)	$ (1.21)

	2018			
	Q4	Q3	Q2	Q1
Related party revenue	$ 47,119	$ 20,815	$ 22,118	$ 18,613
Income (loss) from operations	13,056	(8,469)	(4,186)	(4,715)
Net income (loss)	14,165	(7,517)	(3,200)	(3,941)
Net loss per share, basic and diluted (1),(3)	$ —	$ (1.15)	$ (0.52)	$ (0.64)

(1) Through the application of the two-class method, all undistributed earnings were allocated to then outstanding convertible preferred stock for the three months ended December 31, 2018.
(2) On March 22, 2019, the Company filed an amendment to the Company's amended and restated certificate of incorporation to effect a reverse split of shares of the Company's common stock on a two-for-one basis.
(3) Net loss per common share is computed independently for each of the quarters presented. Therefore, the sum of quarterly Net loss per common share information may not equal annual Net loss per common share.

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

As of December 31, 2019, management, with the participation of our Chief Executive Officer and Acting Chief Financial Officer, performed an evaluation of the effectiveness of the design and operation of our disclosure controls and procedures as defined in Rules 13a-15(e) and 15d-15(e) of the Exchange Act. Our disclosure controls and procedures are designed to ensure that information required to be disclosed in the reports we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including the Chief Executive Officer and Acting Chief Financial Officer, to allow timely decisions regarding required disclosures.

Any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objective and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on this evaluation, our Chief Executive Officer and Acting Chief Financial Officer concluded that, as of December 31, 2019, the design and operation of our disclosure controls and procedures were effective at a reasonable assurance level.

Changes in Internal Control over Financial Reporting

There was no change in our internal control over financial reporting identified in connection with the evaluation required by Rule 13a-15(f) and 15d-15(f) of the Exchange Act that occurred during the year ended December 31, 2019 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Management's Report on Internal Control Over Financial Reporting

This Annual Report on Form 10-K does not include a report of management's assessment regarding internal control over financial reporting or an attestation report of our independent registered public accounting firm due to a transition period established by the rules of the SEC for newly public companies.

Item 9B. Other Information.

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

Information required by this item regarding directors and director nominees, executive officers, the board of directors and its committees, and certain corporate governance matters is incorporated by reference to the information set forth under the captions “Proposal No. 1—Election of Directors,” “Corporate Governance and Board Matters” and “Executive Officers” in our Proxy Statement for our 2020 Annual Meeting of Stockholders. Information required by this item regarding compliance with Section 16(a) of the Exchange Act is incorporated by reference to the information set forth under the caption “Security Ownership of Certain Beneficial Owners and Management” in our Proxy Statement.

Our written code of business conduct and ethics (the “Code of Conduct”) applies to all of our employees, officers and directors, including our principal executive officer, principal financial officer and principal accounting officer or controller. The Code of Conduct is available on our corporate website at https://www.ngmbio.com/ in the Investors & Media section under “Corporate Governance.” If we make any substantive amendments to our Code of Conduct or grant any of our directors or executive officers any waiver, including any implicit waiver, from a provision of our Code of Conduct, we will disclose the nature of the amendment or waiver on our website or in a Current Report on Form 8-K.

Item 11. Executive Compensation.

Information required by this item regarding executive compensation is incorporated by reference to the information set forth under the captions “Executive Compensation” and “Director Compensation” in our Proxy Statement.

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

Information required by this item regarding security ownership of certain beneficial owners and management is incorporated by reference to the information set forth under the caption “Security Ownership of Certain Beneficial Owners and Management” and “Equity Compensation” in our Proxy Statement.

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

Information required by this item regarding certain relationships, related transactions and director independence is incorporated by reference to the information set forth under the caption “Transactions with Related Persons and Indemnification” and “Corporate Governance and Board Matters” in our Proxy Statement.

Item 14. Principal Accounting Fees and Services.

Information required by this item regarding principal accounting fees and services is incorporated by reference to the information set forth under the caption “Proposal No. 2—Ratification of Selection of Independent Registered Public Accounting Firm” in our Proxy Statement.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

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

1. *Financial Statements.* See Index to Financial Statements in Part II Item 8 of this Annual Report on Form 10-K.

2. *Financial Statement Schedules*. None. All financial statement schedules are omitted because they are not applicable, not required under the instructions, or the requested information is included in the consolidated financial statements or notes thereto.

3. *Exhibits*. The following is a list of exhibits filed with this Annual Report or incorporated herein by reference:

		Incorporated by Reference				
Exhibit Number	**Exhibit Description**	**Form**	**File No.**	**Exhibit**	**Filing Date**	**Filed Herewith**
3.1	Amended and Restated Certificate of Incorporation.	8-K	001-38853	3.1	4/8/19	
3.2	Amended and Restated Bylaws.	S-1	333-227608	3.4	9/28/18	
4.1	Amended and Restated Investors' Rights Agreement among the Registrant and certain of its stockholders, dated March 20, 2015.	S-1	333-227608	4.1	9/28/19	
4.2	Form of Common Stock Certificate.	S-1	333-227608	4.2	4/1/19	
4.3	Description of Capital Stock.					X
10.1*	2008 Equity Incentive Plan, as amended.	S-1	333-227608	10.1	9/28/18	
10.2*	Form of Stock Option Agreement and Stock Option Grant Notice under the 2008 Equity Incentive Plan.	S-1	333-227608	10.2	9/28/18	
10.3*	Amended and Restated 2018 Equity Incentive Plan.	S-1	333-227608	10.3	3/25/19	
10.4*	Forms of Stock Option Agreement and Notice of Grant of Stock Option under the Amended and Restated 2018 Equity Incentive Plan.	S-1	333-227608	10.4	3/25/19	
10.5*	Forms of Restricted Stock Unit Agreement and Notice of Grant of Restricted Stock Unit under the Amended and Restated 2018 Equity Incentive Plan.	S-1	333-227608	10.5	3/25/19	
10.6*	2019 Employee Stock Purchase Plan.	S-1	333-227608	10.6	3/25/19	
10.7*	Form of Indemnification Agreement, by and between NGM Biopharmaceuticals, Inc. and each of its directors and executive officers.	S-1	333-227608	10.7	9/28/18	
10.8*	NGM Biopharmaceuticals, Inc. Non-Employee Director Compensation Policy.	S-1	333-227608	10.8	3/25/19	

10.9	Sublease Agreement, by and between NGM Biopharmaceuticals, Inc. and AMGEN Inc., dated December 11, 2015.	S-1	333-227608	10.9	9/28/18	
10.10*	Executive Employment Offer Letter, by and between NGM Biopharmaceuticals, Inc. and Jin-Long Chen, Ph.D.	S-1	333-227608	10.11	9/28/18	
10.11*	Executive Employment Offer Letter, by and between NGM Biopharmaceuticals, Inc. and Aetna Wun Trombley, Ph.D.	S-1	333-227608	10.12	3/25/19	
10.12*	Executive Employment Agreement, by and between NGM Biopharmaceuticals, Inc. and David Woodhouse, Ph.D.	S-1	333-227608	10.13	3/25/19	
10.13#	Research Collaboration, Product Development and License Agreement by and between NGM Biopharmaceuticals, Inc. and Merck Sharp & Dohme Corp., dated as of February 18, 2015.	S-1	333-227608	10.15	9/28/18	
10.14#	First Amendment to Research Collaboration, Product Development and License Agreement by and between NGM Biopharmaceuticals, Inc. and Merck Sharp & Dohme Corp., dated as of January 1, 2016.	S-1	333-227608	10.16	9/28/18	
10.15	Letter Agreement, by and between NGM Biopharmaceuticals, Inc. and Merck Sharp & Dohme Corp., dated as of March 20, 2015.	S-1	333-227608	10.17	9/28/18	
10.16#	Multi-Product Licence Agreement by and between NGM Biopharmaceuticals, Inc. and Lonza Sales AG, dated as of October 31, 2014, as amended by Amendment No. 1 on July 28, 2015, Amendment No. 2 on October 7, 2015, Amendment No. 3 on April 26, 2016, Amendment No. 4 on October 3, 2017, Amendment No. 5 on March 16, 2018 and Amendment No. 6 on February 6, 2019.	S-1	333-227608	10.17	4/1/19	
10.17	Letter Agreement, by and between NGM Biopharmaceuticals, Inc. and Merck Sharp & Dohme Corp., dated as of March 15, 2019.	S-1	333-227608	10.18	3/25/19	
21.1	Subsidiaries of NGM Biopharmaceuticals, Inc.					X
23.1	Consent of Independent Registered Public Accounting Firm.					X
24.1	Power of Attorney (included on signature page).					X
31.1	Certification of Chief Executive Officer and Acting Chief Financial Officer pursuant to Exchange Act Rules 13a-14(a) and 15d-14(a), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.					X

32.1†	Certification of Chief Executive Officer and Acting Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	X
101.INS	XBRL Instance Document.	X
101.SCH	XBRL Taxonomy Extension Schema Document.	X
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document	X
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document	X
101.LAB	XBRL Taxonomy Extension Label Linkbase Document	X
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document	X

* Indicates management contract or compensatory plan or arrangement.

\# Confidential treatment has been granted for a portion of this exhibit.

† The certifications attached as Exhibit 32.1 accompany this Annual Report on Form 10-K are not deemed filed with the Securities and Exchange Commission and are not to be incorporated by reference into any filing of NGM Biopharmaceuticals, 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 this Annual Report on Form 10-K, irrespective of any general incorporation language contained in such filing.

Item 16. Form 10-K Summary.

None.

SIGNATURES

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

NGM Biopharmaceuticals, Inc.

Date: March 17, 2020

By: /s/ David J. Woodhouse, Ph.D.
David J. Woodhouse, Ph.D.
Chief Executive Officer and Acting Chief Financial Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints William J. Rieflin and David J. Woodhouse, and each of them, as his or her true and lawful attorneys-in-fact and agents, with full power of substitution for him or her, and in his or her 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 U.S. Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, 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 or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, and either of them, his or her 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 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/ David J. Woodhouse, Ph.D. David J. Woodhouse, Ph.D.	Chief Executive Officer, Acting Chief Financial Officer and Director *(principal executive officer, principal financial officer and principal accounting officer)*	March 17, 2020
/s/ William J. Rieflin William J. Rieflin	Executive Chairman and Director	March 17, 2020
/s/ Jin-Long Chen Jin-Long Chen, Ph.D.	Chief Scientific Officer and Director	March 17, 2020
/s/ David V. Goeddel David V. Goeddel, Ph.D.	Director	March 17, 2020
/s/ Shelly D. Guyer Shelly D. Guyer	Director	March 17, 2020
/s/ Suzanne Sawochka Hooper Suzanne Sawochka Hooper	Director	March 17, 2020
/s/ Mark Leschly Mark Leschly	Director	March 17, 2020
/s/ David Schnell David Schnell, M.D.	Director	March 17, 2020
 Peter Svennilson	Director	
/s/ McHenry T. Tichenor, Jr. McHenry T. Tichenor, Jr.	Director	March 17, 2020

Exhibit 4.3

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

NGM Biopharmaceuticals, Inc. ("we," "our," "us," or the "Company") has one class of securities registered under Section 12 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"): our common stock. The following summary of the terms of our common stock is based upon our amended and restated certificate of incorporation and our amended and restated bylaws, which are filed as exhibits to our Annual Report on Form 10-K, of which this Exhibit 4.3 is a part, and are incorporated by reference herein. This summary does not purport to be complete and is subject to, and is qualified in its entirety by express reference to, the applicable provisions of our amended and restated certificate of incorporation and our amended and restated bylaws. We encourage you to read our amended and restated certificate of incorporation and our amended and restated bylaws and the applicable provisions of the Delaware General Corporation Law (the "DGCL") for more information. We also provide a summary of our preferred stock, which is not registered under Section 12 of the Exchange Act.

DESCRIPTION OF CAPITAL STOCK

General

Our amended and restated certificate of incorporation provides for one class of common stock and undesignated preferred stock, the rights, preferences and privileges of which may be designated from time to time by our board of directors.

Our amended and restated certificate of incorporation authorizes us to issue up to 400,000,000 shares of common stock, par value $0.001 per share, and 10,000,000 shares of preferred stock, par value $0.001 per share.

Common Stock

Voting Rights

Each holder of common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders. In addition to any vote of holders of a specific class or series, or required by law or the amended and restated certificate of incorporation, the affirmative vote of holders of at least 66 2/3% of the voting power of all of the then outstanding shares of capital stock, voting as a single class, is required to amend certain provisions of our amended and restated certificate of incorporation, including provisions relating to amending our amended and restated bylaws, the classified board, the size of our board, removal of directors, director liability, vacancies on our board, special meetings, stockholder notices, actions by written consent and exclusive jurisdiction.

Dividends

Subject to preferences that may apply to any outstanding convertible preferred stock, holders of our common stock are entitled to receive ratably any dividends that our board of directors may declare out of funds legally available for that purpose.

Liquidation

In the event of our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preference of any outstanding convertible preferred stock.

Rights and Preferences

Holders of our common stock have no preemptive, conversion, subscription or other rights, and there are no redemption or sinking fund provisions applicable to our common stock. The rights, preferences and privileges of the holders of our common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of our convertible preferred stock that we may designate in the future.

Fully Paid and Nonassessable

All outstanding shares of our common stock are fully paid and nonassessable.

Preferred Stock

Our board of directors has the authority, without further action by our stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series and to fix the number, rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences and 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 common stock. The issuance of our preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change in control or other corporate action.

Anti-Takeover Provisions

Certificate of Incorporation and Bylaws

Our amended and restated certificate of incorporation and amended and restated bylaws include a number of provisions that may deter or impede hostile takeovers or changes of control or management. These provisions include:

- ***Issuance of Undesignated Preferred Stock:*** Our board of directors has the authority, without further action by the stockholders, to issue up to 10,000,000 shares of undesignated preferred stock with rights and preferences, including voting rights, designated from time to time by our board of directors. The existence of authorized but unissued shares of preferred stock enables our board of directors to make it more difficult to attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise.

- ***Classified Board:*** Our amended and restated certificate of incorporation provides for a classified board of directors consisting of three classes of directors, with staggered three-year terms. Only one class of directors will be elected at each annual meeting of our stockholders, with the other classes continuing for the remainder of their respective three-year terms. This provision may have the effect of delaying a change in control of our board.

- ***Board of Directors Vacancies:*** Our amended and restated certificate of incorporation and amended and restated bylaws authorize only our board of directors to fill vacant directorships. In addition, the number of directors constituting our board of directors may be set only by resolution adopted by a majority vote of our entire board of directors. These provisions prevent a stockholder from increasing the size of our board of directors and gaining control of our board of directors by filling the resulting vacancies with its own nominees.

- ***Stockholder Action; Special Meetings of Stockholders:*** Our amended and restated certificate of incorporation provides that our stockholders may not take action by written consent, but may only take action at annual or special meetings of our stockholders. Stockholders are not permitted to cumulate their votes for the election of directors. Our amended and restated bylaws provide that only the chairman of our board of directors, our chief executive officer, or a majority of our board of directors may call special meetings of our stockholders.

- ***Advance Notice Requirements for Stockholder Proposals and Director Nominations:*** Our amended and restated bylaws provide advance notice procedures for stockholders seeking to bring business before our annual meeting of stockholders, or to nominate candidates for election as directors at our annual meeting of stockholders. Our amended and restated bylaws also specify certain requirements as to the form and content of a stockholder's notice. These provisions may make it more difficult for our stockholders to bring matters before our annual meeting of stockholders or to nominate directors at annual meetings of stockholders.

We designed these provisions to enhance the likelihood of continued stability in the composition of our board of directors and its policies, to discourage certain types of transactions that may involve an actual or threatened acquisition of us and to reduce our vulnerability to an unsolicited acquisition proposal. We also designed these provisions to discourage certain tactics that may be used in proxy fights. However, these provisions could have the effect of discouraging others from making tender offers for our shares and, as a consequence, they may also reduce fluctuations in the market price of our shares that could result from actual or rumored takeover attempts.

Section 203 of the Delaware General Corporation Law

We are subject to Section 203 of the DGCL, which prohibits a Delaware corporation from engaging in a business combination with any interested stockholder for a period of three years following the date the person became an interested stockholder, with the following exceptions:

- before such date, the board of directors of the corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested holder;

- upon completion of the transaction that 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 began, excluding for purposes of determining the voting stock outstanding (but not the outstanding voting stock owned by the interested stockholder) those shares owned (a) by persons who are directors and also officers and (b) pursuant to employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; and

- on or after such date, the business combination is approved by the board of directors and authorized at an annual or special meeting of the stockholders, and not by written consent, by the affirmative vote of at least 66⅔% of the outstanding voting stock that is not owned by the interested stockholder.

In general, Section 203 of the DGCL defines business combination to include the following:

- any merger or consolidation involving the corporation and the interested stockholder;

- any sale, lease, transfer, pledge or other disposition of 10% or more of the assets of the corporation involving the interested stockholder;

- subject to certain exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;

- 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; and

- 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 of the DGCL defines an interested stockholder as an entity or person who, together with the entity's or person's affiliates and associates, beneficially owns, or is an affiliate of the corporation and within three years prior to the time of determination of interested stockholder status did own, 15% or more of the outstanding voting stock of the corporation.

A Delaware corporation may opt out of these provisions with an express provision in its certificate of incorporation. We have not opted out of these provisions, which may as a result, discourage or prevent mergers or other takeover or change in control attempts of us.

Choice of Forum

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware will be the exclusive forum for the following types of actions or proceedings under Delaware statutory or common law: (i) any derivative action or proceeding brought on our behalf; (ii) any action asserting a breach of fiduciary duty owed by any director, officer or other employee to us or our stockholders; (iii) any action asserting a claim against us or any director or officer or other employee arising pursuant to the Delaware General Corporation Law, our amended and restated certificate of incorporation or amended and restated bylaws; or (iv) any action asserting a claim against us or any director or officer or other employee that is governed by the internal affairs doctrine. This provision would not apply to claims brought to enforce a duty or liability created by the Exchange Act or any other claim for which the federal courts have exclusive jurisdiction. Our amended and restated certificate of incorporation further provides that the federal district courts of the United States of America will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act, subject to and contingent upon a final adjudication in the State of Delaware of the enforceability of such exclusive forum provision.

Transfer Agent and Registrar

Our transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC. The transfer agent's address is 6201 15th Avenue, Brooklyn, New York 11219.

The Nasdaq Global Select Market

Our common stock is listed on the Nasdaq Global Select Market under the trading symbol "NGM."

Exhibit 21.1

SUBSIDIARIES

Subsidiary Name	Jurisdiction of Incorporation or Organization
NGM Biopharmaceuticals Australia Pty Ltd.	Australia

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the Registration Statement (Form S-8 No. 333-230725) pertaining to NGM Biopharmaceuticals, Inc. Amended and Restated 2018 Equity Incentive Plan and NGM Biopharmaceuticals, Inc. 2019 Employee Stock Purchase Plan of NGM Biopharmaceuticals, Inc. of our report dated March 17, 2020, with respect to the consolidated financial statements of NGM Biopharmaceuticals, Inc., included in this Annual Report (Form 10-K) for the year ended December 31, 2019.

/s/ Ernst & Young LLP

Redwood City, California
March 17, 2020

Exhibit 31.1

CERTIFICATION PURSUANT TO
RULES 13A-14(A) AND 15D-14(A) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, David J. Woodhouse, certify that:

1. I have reviewed this Annual Report on Form 10-K of NGM Biopharmaceuticals, Inc.;

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

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

4. I am responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

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

   (b) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report my 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

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

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

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

Date: March 17, 2020

By: /s/ David J. Woodhouse, Ph.D.
David J. Woodhouse, Ph.D.
Chief Executive Officer and Acting Chief Financial Officer
(Principal Executive Officer and Principal Financial 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

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, (the "Exchange Act") and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. § 1350), David J. Woodhouse, Principal Executive Officer and Principal Financial Officer of NGM Biopharmaceuticals, Inc. (the "Company") hereby certifies that, to the best of his knowledge:

1. The Company's Annual Report on Form 10-K for the year ended December 31, 2019, to which this Certification is attached as Exhibit 32.1 (the "Annual Report"), fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act; and

2. The information contained in the Annual Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 17, 2020

/s/ David J. Woodhouse, Ph.D.
David J. Woodhouse, Ph.D.
Chief Executive Officer and Acting Chief Financial Officer
(Principal Executive Officer and Principal Financial Officer)

This certification accompanies the Annual Report on 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 NGM Biopharmaceuticals, Inc. under the Securities Act of 1933, as amended, or the Exchange Act (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing. A signed original of this written statement required by Section 906, or other document authenticating, acknowledging, or otherwise adopting the signature that appears in typed form within the electronic version of this written statement required by Section 906, has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.