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

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2019

OR

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

Commission File Number 001-39122

89bio, Inc.

(Exact name of Registrant as specified in its Charter)

Delaware	**36-4946844**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
142 Sansome Street, Second Floor San Francisco, California 94104	**94104**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (415) 500-4614

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common stock, par value $0.001 per share	ETNB	Nasdaq Global Market

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

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

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 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, 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 Exchange Act). YES ☐ NO ☒

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant as of March 2, 2020 was approximately $169,328,521, based on the closing price on The Nasdaq Global Market reported for such date. Shares of common stock held by each officer and director and by each person who is known to own 10% or more of the outstanding common stock have been excluded in that such persons may be deemed to be affiliates of the Registrant. This determination of affiliate status is not necessarily a conclusive determination for other purposes. The Registrant has elected to use March 2, 2020 as the calculation date, as on the last business day of the Registrant's most recently completed second fiscal quarter there was no public market for the Registrant's common stock.

As of March 10, 2020, there were 13,788,982 shares of the Registrant's common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

None.

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FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains "forward-looking statements" within the meaning of the federal securities laws, which statements involve substantial risks and uncertainties. All statements, other than statements of historical facts included in this Annual Report on Form 10-K, including statements concerning our plans, objectives, goals, strategies, future events, future revenues or performance, financing needs, plans or intentions relating to acquisitions, business trends and other information referred to in "Business," "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" are forward-looking statements. Forward-looking statements generally relate to future events or our future financial or operating performance. In some cases, you can identify forward-looking statements by terms such as "may," "might," "will," "objective," "intend," "should," "could," "can," "would," "expect," "believe," "design," "estimate," "predict," "potential," "plan," "anticipate," "target," "forecast," or the negative of these terms, and similar expressions intended to identify forward-looking statements. Forward-looking statements are not historical facts and reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties. Given these uncertainties, you should not place undue reliance on these forward-looking statements.

There are a number of risks, uncertainties and other important factors that could cause our actual results to differ materially from the forward-looking statements contained in this Annual Report on Form 10-K. Such risks, uncertainties and other important factors include, among others, the risks, uncertainties and factors set forth in "Risk Factors," and the following risks, uncertainties and factors:

- our plans to develop and commercialize BIO89-100 or any future product candidates;
- our ongoing and planned clinical trials;
- the timing of and our ability to obtain regulatory approvals for BIO89-100 or any future product candidates;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- our ability to identify additional products or product candidates with significant commercial potential that are consistent with our commercial objectives;
- the rate and degree of market acceptance and clinical utility of BIO89-100 or any future product candidates, if approved;
- our commercialization, marketing and manufacturing capabilities and strategy;
- significant competition in our industry;
- our intellectual property position;
- loss of key members of management;
- failure to successfully execute our growth strategy, including any delays in our planned future growth; and
- our failure to maintain effective internal controls.

There may be other factors that may cause our actual results to differ materially from the forward-looking statements, including factors disclosed in "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations." You should evaluate all forward-looking statements made in this Annual Report on Form 10-K in the context of these risks and uncertainties.

We caution you that the risks, uncertainties and other factors referred to above may not contain all of the risks, uncertainties and other factors that are important to you. In addition, we cannot assure you that we will realize the results, benefits or developments that we expect or anticipate or, even if substantially realized, that they will result in the consequences or affect us or our business in the way expected. All forward-looking statements in this Annual Report on Form 10-K apply only as of the date made and are expressly qualified in their entirety by the cautionary statements included in this Annual Report on Form 10-K. We undertake no obligation to publicly update or revise any forward-looking statements to reflect subsequent events or circumstances.

PART I

In this Annual Report on Form 10-K, unless context otherwise requires or where otherwise indicated, the terms "89bio" "we," "us," "our," "our company," "the company," and "our business" refer to 89bio, Inc. and its consolidated subsidiaries.

Item 1. Business.

Overview

We are a clinical-stage biopharmaceutical company focused on the development and commercialization of innovative therapies for the treatment of liver and cardio-metabolic diseases. Our lead product candidate, BIO89-100, a specifically engineered glycoPEGylated analog of fibroblast growth factor 21 (" FGF21"), is currently being developed for the treatment of nonalcoholic steatohepatitis ("NASH"). NASH is a severe form of nonalcoholic fatty liver disease ("NAFLD"), characterized by inflammation and fibrosis in the liver that can progress to cirrhosis, liver failure, hepatocellular carcinoma ("HCC") and death. There are currently no approved products for the treatment of NASH. FGF21 is a clinically-validated mechanism that has been shown in humans to reduce steatosis and address cardio-metabolic dysregulation. We believe BIO89-100 may be a differentiated FGF21 therapy based on its robust and durable biological effects and a favorable tolerability profile, as well its potential for a longer dosing interval. Combining these characteristics with the ability to address the key liver pathologies in NASH, as well as the underlying metabolic dysregulation in NASH patients, BIO89-100 has the potential to become a mainstay of NASH therapy. We successfully completed a Phase 1a, first-in-human, SAD clinical trial with 58 healthy volunteers. The magnitude and significance of BIO89-100's biological effects after a single dose on lipid parameters were robust and durable. In July 2019, we initiated our proof of concept ("POC") Phase 1b/2a clinical trial in patients with NASH or patients with NAFLD and a high risk of NASH and we expect to report topline data in the second half of 2020. We also intend to develop BIO89-100 for the treatment of severe hypertriglyceridemia ("SHTG"), a condition identified by severely elevated levels of triglycerides (greater than or equal to 500 mg/dL), which is associated with an increased risk of NASH, cardiovascular events and acute pancreatitis. We expect to initiate our Phase 2 trial in SHTG patients in the first half of 2020 in order to evaluate the ability of BIO89-100 to reduce fasting plasma triglyceride levels compared to baseline levels and to report topline data in the first half of 2021. Based on the U.S. Food and Drug Administration ("FDA") guidance for the development of SHTG treatments, as well as the regulatory path followed by other companies that have successfully developed SHTG therapies, we believe that a combination of smaller clinical trials and shorter development timelines could mean that SHTG potentially represents a quicker path to market for BIO89-100. We believe BIO89-100 has the potential to address multiple drivers underlying metabolic dysregulation, which would make it an ideal candidate for selected liver and cardio-metabolic diseases.

The prevalence of NAFLD, which affects approximately 25% of the global population, and NASH, which develops in approximately 20% to 25% of NAFLD patients, is growing and is driven primarily by the worldwide obesity epidemic. NAFLD and NASH patients have an excessive accumulation of fat in the liver resulting primarily from a caloric intake above and beyond energy needs. In NAFLD patients, this abnormal liver fat contributes to the progression to NASH, a liver necro-inflammatory state, that can lead to scarring, also known as fibrosis, and, for some, can progress to cirrhosis and liver failure. The critical pathophysiologic mechanisms underlying the development and progression of NASH include reduced ability to handle lipids, increased insulin resistance, injury to hepatocytes and liver fibrosis in response to hepatocyte injury. Patients with NASH frequently have other significant metabolic co-morbidities such as obesity, hyperglycemia, dyslipidemia and systemic hypertension (a constellation of which is commonly referred to as metabolic syndrome) and these further contribute to the risk of cardiovascular disease. The number of NASH cases in the United States is projected to expand from 16.5 million in 2015 to 27 million in 2030, with similar prevalence growth expected in Europe. Diet and exercise are currently the standard of care for NAFLD and NASH, but adherence to this treatment regimen is poor and there remains a high unmet need in the treatment of NASH.

BIO89-100 is a specifically engineered FGF21 analog that we believe has the potential to address the critical pathophysiologic mechanisms underlying NASH. FGF21 is a metabolic hormone that regulates energy expenditure and glucose and lipid metabolism. FGF21 has been clinically shown to reduce steatosis in the liver. It is also thought to exert effects on liver fibrosis by improving metabolic regulation, which reduces ongoing liver injury thus giving the liver time to heal. FGF21 also generates an on-target effect to increase adiponectin, a hormone released from adipose tissue that, among other functions, can suppress development and progression of hepatic fibrosis. However, FGF21 in its native form suffers from a short half-life and a tendency to aggregate in solution, both of which impact its suitability as a viable drug. To address these challenges, we have specifically engineered BIO89-100 to maintain the clinical benefits of FGF21, while extending half-life in vivo, protecting against proteolysis, reducing renal clearance, minimizing susceptibility to aggregate in solution and optimizing potency.

BIO89-100 has been evaluated in seven animal studies of NASH, diabetes and obesity, including studies in mice and non-human primates. Each study was customized to assess endpoints relevant to liver and metabolic diseases and conducted according to standard practices at experienced contract research organizations ("CROs"). In these preclinical studies, consistent beneficial effects across a range of endpoints were observed, including improvements in hepatic steatosis, injury and fibrosis in a diet-induced NASH study of 50 mice (see "BIO89-100—Results of DIN Mouse Studies" Figure 11 which illustrates that statistically significant mean changes with respect to hepatic steatosis and fibrosis were each observed and Figure 12 which illustrates that statistically significant mean changes with respect to injury were observed) and improved glycemic control and lipid handling in a study of 24 spontaneously diabetic obese cynomolgus monkeys with elevated triglycerides (see "BIO89-100—Results of Spontaneously Diabetic Obese Cynomolgus Monkey Studies" Figures 20 and 21, respectively, which illustrate that statistically significant mean changes with respect to glycemic control and lipid handling were each observed). We believe this demonstrates BIO89-100's potential to simultaneously address the multiple drivers of NASH pathogenesis. The histological endpoints assessed in these preclinical studies, NAFLD activity score ("NAS") and fibrosis score, mirror the endpoints we expect to assess in our clinical development. In addition, treatment with BIO89-100 in animal models demonstrated consistent reductions in body weight.

In May 2019, we announced positive topline data from our Phase 1a, first-in-human, SAD clinical trial of BIO89-100 in 58 healthy volunteers. In this SAD study, BIO89-100 demonstrated a favorable tolerability profile in the 43 volunteers who received BIO89-100 with a half-life of 55 to 100 hours. At single doses of 9.1 mg and higher, BIO89-100 demonstrated significant improvements in key lipid parameters measured at Day 8 and Day 15 after dosing on Day 1. The mean changes versus baseline include reductions in triglycerides (up to 51%) and LDL-C (up to 37%) and increase in HDL-C (up to 36%) despite the baseline values being in the normal range. As compared to placebo treatment, these mean changes were all statistically significant ($p < 0.001$). BIO89-100 demonstrated rapid (beginning from Day 2), sustained and durable improvements in lipid parameters for two weeks or more after single dose administration. Based on these findings and results from our animal studies, we believe such a lengthy duration of effect may confer longer dosing intervals to BIO89-100.

In the second quarter of 2020, we expect to complete patient enrollment in our POC Phase 1b/2a trial with 83 total patients randomized to receive once weekly or once every two weeks subcutaneous dosing of either BIO89-100 or placebo, in each case, for up to 12 weeks.

This trial is designed to assess the safety, tolerability and PK properties of BIO89-100, as well as changes in liver steatosis and key biomarker assessments.

We also intend to develop BIO89-100 for the treatment of SHTG, a condition identified by severely elevated levels of triglycerides (greater than or equal to 500 mg/dL) and which is associated with an increased risk of NASH, cardiovascular events and acute pancreatitis. SHTG accounts for up to 10% of all acute pancreatitis episodes. It is estimated that there are 2.5 million to 4 million patients in the United States with TG ≥ 500 mg/dL and up to 50% of SHTG patients treated with certain approved drugs are refractory to current standard of care. In a study of 24 diabetic obese cynomolgus monkeys with elevated triglycerides, BIO89-100 showed significant effects on triglycerides at doses as low as 0.1 mg/kg/week, with a 78% reduction from baseline (range of 52% reduction to 94% reduction) observed at the highest dose level of 1.0 mg/kg/week on Day 56. In our Phase 1a SAD study, BIO89-100 showed a significant reduction in triglycerides of up to 51% after a single dose in healthy volunteers. While currently approved SHTG therapies decrease TG levels, they generally do not have broader metabolic benefits. To the extent that we are able to show in subsequent human clinical trials that BIO89-100 significantly decreases both TG and LDL-C levels and improves other metabolic parameters, we believe that BIO89-100 could be a differentiated therapy in this indication. We expect to initiate our Phase 2 trial in SHTG patients in the first half of 2020 in order to evaluate the ability of BIO89-100 to reduce fasting plasma triglyceride levels compared to baseline levels and to report topline data in the first half of 2021.

We retain exclusive worldwide rights to BIO89-100. BIO89-100 is protected by a family of issued patents with claims directed to composition of matter and methods of use. The first of our patents for BIO89-100 are projected to expire in the United States in 2028, with the final composition-of-matter patent projected to expire in the United States in 2038, in each case, without patent term extensions. Because BIO89-100 is a biologic drug, marketing approval is also expected to provide 12 years of market exclusivity in the United States from the approval date of a BLA. We license the patents and know-how related to the glycoPEGylation technology for use in the research, development, manufacture and commercialization of BIO89-100 from Teva and ratiopharm GmbH ("ratiopharm").

Strategy

Our goal is to become a leading biopharmaceutical company focused on the development and commercialization of innovative therapies for the treatment of liver and cardio-metabolic diseases. The key components of our strategy are to:

- **Rapidly advance BIO89-100 through clinical development for the treatment of NASH.** We believe BIO89-100 may be a differentiated FGF21 therapy based on its robust and durable biological effects and a favorable tolerability profile, as its potential for a longer dosing interval, and is well positioned to address the complex pathophysiology of NASH. In the second quarter of 2020, we expect to complete patient enrollment in our POC Phase 1b/2a clinical trial to evaluate the safety and efficacy of BIO89-100. We believe that our trial design and the use of well-established surrogate clinical endpoints can contribute meaningfully to the rapid advancement of BIO89-100 through its clinical development. With potential for BIO89-100 to be established as a mainstay monotherapy for NASH, we continue to explore opportunities to combine BIO89-100 with products targeting other pathways within NASH for possible development as a combination therapy.
- **Expand the breadth of indications for BIO89-100 with an initial focus on SHTG.** While we are focused on becoming a leader in the treatment of NASH, the mechanism of action of our FGF21 analog supports evaluation across a spectrum of liver and cardio-metabolic diseases. We believe BIO89-100's mechanism and potentially robust and durable biological effects and favorable tolerability profile, as well as its potential for a longer dosing interval make it an ideal candidate for selected liver and cardio-metabolic diseases. We intend to develop BIO89-100 for the treatment of SHTG. Based on FDA guidance for the development of SHTG treatments, as well as the regulatory path followed by other companies that have successfully developed SHTG therapies, we believe that a combination of smaller clinical trials and shorter development timelines could mean that SHTG potentially represents a quicker path to market for BIO89-100.
- **Scale-up and optimize the manufacturing of BIO89-100.** We currently use an external contract manufacturing organization ("CMO") to manufacture BIO89-100 for our ongoing and planned clinical trials. While these trials are ongoing, we plan to work with our CMO to optimize and scale-up the manufacturing process for BIO89-100 to support the increased production that will be needed for later-stage clinical trials and commercialization, if BIO89-100 is approved.
- **Establish a commercial infrastructure in key geographies.** We have worldwide rights to BIO89-100 and intend to develop the sales infrastructure required for commercialization in the United States. We also plan to evaluate options, including strategic collaborations, for commercializing BIO89-100, if approved, in other key markets, such as Europe and China.
- **Construct a diversified multi-asset pipeline of novel therapies.** We intend to employ a value-driven strategy to identify, acquire, develop and commercialize product candidates for liver and cardio-metabolic diseases. We intend to focus on product candidates that we believe have attractive profiles in early clinical testing, address a clear unmet medical need and can advance quickly and efficiently into late-stage development.

Our Focus on Liver and Cardio-Metabolic Disease

We are focused on developing and commercializing therapeutic interventions that have a clinically meaningful impact on patients with liver and cardio-metabolic diseases. These diseases, including NASH and SHTG, represent leading global causes of morbidity and mortality. 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 diseases, there is a significant unmet medical need for more effective therapies to improve patient outcomes and reduce the burden on global healthcare systems.

We are currently developing our lead product candidate, BIO89-100, a specifically engineered glycoPEGylated analog of FGF21, for the treatment of NASH. We believe BIO89-100 is an ideal candidate for the treatment of NASH based on:

- its ability to address the key liver pathologies in NASH;
- its ability to address the underlying metabolic dysregulation in NASH patients;
- its balance of its robust and durable biological effects and favorable tolerability profile; and
- its potential for a longer dosing interval.

Given the potential of BIO89-100 to meaningfully reduce triglycerides, we also intend to develop BIO89-100 for the treatment of SHTG. There is regulatory precedence for the approval of a therapy for the treatment of patients with SHTG in the United States and the reduction in triglycerides from baseline is recognized by the FDA as the primary endpoint for full approval. Based on FDA guidance for the development of SHTG treatments, as well as the regulatory path followed by other companies that have successfully developed SHTG therapies, we believe that a combination of smaller clinical trials and shorter development timelines could mean that SHTG potentially represents a quicker path to market for BIO89-100.

NASH Overview

NAFLD is emerging as the most common chronic liver disorder, driven primarily by the global obesity epidemic. NAFLD affects approximately 25% of the population globally and is often referred to as the hepatic manifestation of metabolic syndrome. Patients with NAFLD have an excessive accumulation of fat in the liver resulting from a caloric intake above and beyond energy needs. This abnormal fat in the liver contributes to the progression of NAFLD to NASH, a necro-inflammatory state in the liver that ultimately leads to scarring, also known as fibrosis; and for certain patients, progression to cirrhosis and liver failure.

Patients with NASH exhibit suboptimal lipid handling, increased insulin resistance, caloric overload and inadequate fat burning, all of which contribute to the increased risk of cardiovascular disease. Due to an increase in obesity and Type 2 diabetes, which predispose individuals to more significant liver disease, the number of NASH cases in the United States is projected to expand from 16.5 million in 2015 to 27 million in 2030.

Currently, there are no approved products for the treatment of NASH and diet and exercise is established as the standard of care.

Disease Overview

NAFLD is a condition of excess fat accumulation, or steatosis, of more than 5% in liver cells, also known as hepatocytes. NASH, a severe form of NAFLD, is characterized histologically by the additional presence of inflammation and hepatocellular injury such as visible ballooning and has a significantly worse prognosis, with the potential to progress to liver fibrosis, cirrhosis or HCC. Steatohepatitis is a key catalyst in fibrosis development, and there is a substantial collinearity between the presence of NASH and fibrosis severity. While NAFLD has historically been viewed as benign in terms of liver-related outcomes, recent studies have challenged this notion since patients with NAFLD may develop NASH and fibrosis over time.

Figure 1 below shows the increase in prevalence liver-related mortality rates by fibrosis stage.

Figure 1: Prevalence and Liver-Related Mortality Rate by Fibrosis Stage

It is estimated that 20% to 25% of NAFLD patients progress to NASH. Of those with NASH, cirrhosis develops in approximately 20% and 45% of patients and in some cases, cirrhosis progresses to decompensated cirrhosis, which results in permanent liver damage that can lead to liver failure. In addition, it is estimated that 8% of patients with advanced fibrosis will develop HCC.

There is a high unmet need in the treatment of NASH, and there are currently no approved therapies. In the United States, the number of NASH cases is projected to expand from 16.5 million in 2015 (5.1% of the population) to 27 million in 2030. The expected lifetime economic burden of all patients with NASH in the United States in 2017 is estimated at $223 billion. NASH is currently the second leading cause of liver transplants behind hepatitis C, and is expected to become the leading cause of liver transplants by 2020.

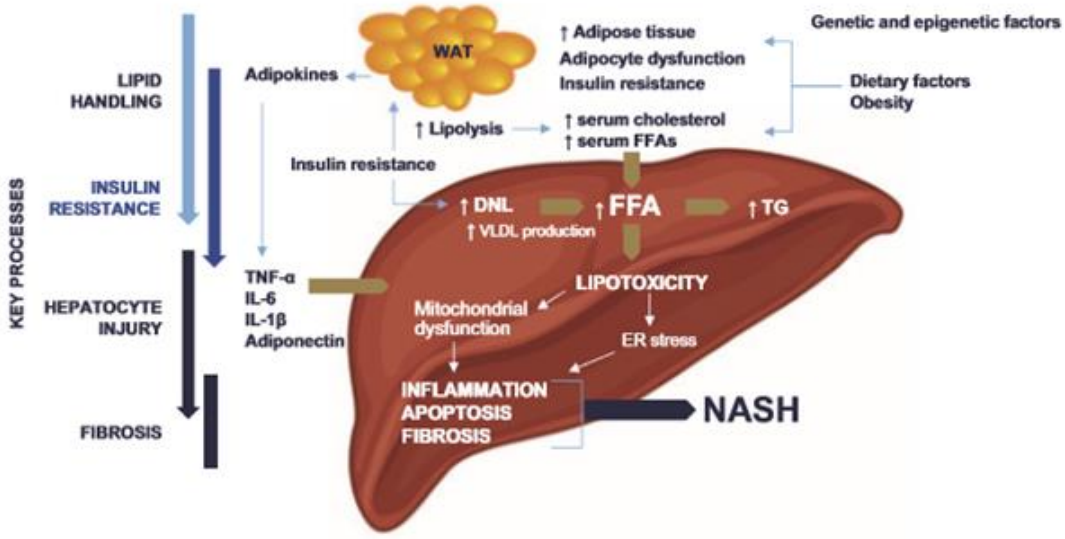
Additionally, multiple epidemiological studies have linked NAFLD to increased cardiovascular disease, concluding that the majority of deaths among NAFLD patients are attributable to cardiovascular disease. As a result, we believe it is important that new therapeutics options for NASH also address the underlying cardiovascular and metabolic dysregulations in these patients.

Etiology

Understanding of the pathophysiologic mechanisms that lead to NASH has evolved in recent years. Excessive caloric overload, metabolic dysregulation, cardio-metabolic co-morbidities and genetic risk factors increase the likelihood of developing NASH, with a multitude of potential mechanistic contributors to pathophysiology. In NASH, the liver's capacity to handle the primary metabolic energy substrates, carbohydrates and fatty acids, is overwhelmed. This occurs when there is an excess of free fatty acids deposited in the liver or their disposal from the liver is impaired. The accumulation of surplus free fatty acids leads to the formation of toxic lipid species. These toxic lipids then induce endoplasmic reticulum stress, oxidative stress and an inflammatory response, which can result in hepatocellular injury and death. This may lead to fibrosis and genomic instability, which may worsen over time to cirrhosis and HCC, respectively.

As shown in Figure 2 below, the critical pathophysiologic mechanisms underlying development and progression of NASH include (1) reduced ability to handle lipids, (2) increased insulin resistance, (3) injury to hepatocytes and (4) development and progression of liver fibrosis in response to hepatocyte injury.

Figure 2: Mechanisms Underlying Development and Progression of NASH



Reduced Ability to Handle Lipids

Excess consumption of calories, poor diet and a sedentary lifestyle, each often associated with obesity, can burden the body with a surplus of carbohydrates and lipids. This burden can be progressively more difficult for the liver to handle thereby resulting in steatosis in the liver. The problem is compounded further as insulin resistance develops.

Free fatty acids (“FFA”) accumulate in the liver primarily from three sources, namely, through (1) the transfer from peripheral adipose tissues where triglycerides are mobilized, (2) de-novo lipogenesis (“DNL”), and (3) direct dietary intake. The FFA that lead to NASH are believed to arise primarily from the peripheral tissue pool and secondarily through DNL. The increase in the influx of FFA to the liver from the peripheral tissues is driven by excessive caloric intake greater than the body’s demand and increased insulin resistance resulting in deposition of fat to the liver for processing. DNL is a distinct process in the liver by which hepatocytes convert excess carbohydrates, especially fructose, to fatty acids.

The three main fates of fatty acids in the liver are (1) mitochondrial beta-oxidation (to release ATP, or energy), (2) re-esterification to form triglyceride, which can then be exported into the blood as very low density lipoproteins, or (3) stored in lipid droplets, resulting in liver steatosis and ultimately NASH. Adiponectin, a hormone derived from adipose tissue, appears to have a pivotal role in improving fatty acid oxidation and decreasing fatty acid synthesis, components of lipid handling.

An increase in cholesterol accumulation in the liver can also contribute to NASH, though its role is not as clearly defined as in the case of triglycerides. The dysregulation of the cholesterol pathway can result in an increase in the cholesterol levels in the liver. The increased cholesterol can accumulate in the liver cell membranes and activate Kupffer cells (activated stellate macrophages), thereby triggering inflammatory pathways and resulting in the progression of NASH.

Increased Insulin Resistance

Insulin resistance, which typically develops in obese individuals, is considered to be a fundamental underlying mechanism in the majority of NASH patients. Fatty acids are primarily delivered to the liver from blood following lipolysis of triglycerides in adipose tissue, a process that is regulated by the actions of insulin on adipocytes. Insulin resistance in adipose tissue manifests as dysregulated lipolysis resulting in excessive delivery of FFA to the liver. The liver tries to cope with the large influx of FFA; however, the build-up of metabolic intermediates interferes with signaling, resulting in hepatic insulin resistance and the inability of the liver to process this excess FFA influx. The state of hepatic insulin resistance further exacerbates the problem by triggering DNL and the build-up of excess fat in the liver.

Injury to Hepatocytes

When the disposal of fatty acids through beta-oxidation or the formation of triglycerides is chronically overwhelmed, fatty acids can form lipotoxic species that lead to stress on the endoplasmic reticulum, oxidative stress and inflammation, all of which are pivotal processes in the development of NASH. Liver inflammation may be an important link between the initial metabolic stress and subsequent hepatocyte death and stimulation of fibrogenesis in NASH by promotion of the expression of pro-inflammatory cytokines and of apoptosis (cell death). These processes are core to the steatohepatitis that gives NASH its name. For example, hepatocyte apoptosis results in the ballooning of cells, a classic pathological feature of NASH. While hepatocytes are the primary and major target of toxic lipids, other cells such as Kupffer cells and hepatic stellate cells are also affected by lipotoxicity and contribute to the development of NASH pathology.

Additional factors, including dysregulation of cytokines and adipokines, energy depletion, anti-oxidant deficiencies, products of the gut microbiome and iron load may modulate hepatocyte vulnerability to the development of lipotoxic stress, injury and inflammation.

Development and Progression of Liver Fibrosis in Response to Hepatocyte Injury

Signaling from stressed or injured hepatocytes and Kupffer cells leads to activation of quiescent hepatic stellate cells. Upon activation, hepatic stellate cells release collagen and other factors. When the production of collagen and matrix proteins is faster than their degradation, accumulation of these proteins in the extracellular matrix can lead to progressive fibrosis. As the lipotoxicity and inflammation continue to damage the liver, the hepatic stellate cells continue to be activated resulting in greater collagen deposition that ultimately leads to fibrosis and cirrhosis.

Co-morbidities Associated with NASH

Patients with NASH frequently have other significant co-morbidities—hypertriglyceridemia, obesity, hyperlipidemia/dyslipidemia, hyperglycemia (including Type 2 diabetes) and systemic hypertension, a constellation of which is commonly referred to as metabolic syndrome—which also increase the risk of developing cardiovascular disease. Figure 3 below shows certain co-morbidities associated with NASH.

Figure 3: NASH Co-morbidities

Selected Co-morbidities	Prevalence in NASH Population
Hypertriglyceridemia	83%
Obesity	82%
Hyperlipidemia / Dyslipidemia	72%
Metabolic syndrome	71%
Type 2 diabetes	44%

The association between NASH and features of metabolic syndrome appears to be bidirectional.

Metabolic syndrome increases the risk of NASH and NASH may also exacerbate several features and co-morbidities of metabolic syndrome. Type 2 diabetes, hypertriglyceridemia, obesity and other features of metabolic syndrome have all been shown to be associated with an increased risk for NASH and advanced liver fibrosis. In addition, it is estimated that approximately 30% of obese patients and approximately 30% of patients with Type 2 diabetes have NASH.

In addition, NASH was found to independently increase the risk of non-liver-related adverse outcomes, including cardiovascular risk and malignancy. Multiple epidemiological studies have linked NASH to increased cardiovascular morbidity, concluding that the majority of deaths among NASH patients are attributable to cardiovascular disease (cardiovascular death is four times higher than death related to liver disease).

In considering therapeutic options to treat NASH, we believe it is important to address the underlying metabolic co-morbidities in addition to the liver pathology.

Diagnosis

Most people with NASH are asymptomatic and their disease is often discovered incidentally following a liver imaging procedure, such as an ultrasound, prescribed for other reasons or as part of an investigation for elevated liver enzymes. Once suspected clinically, a liver biopsy is required to definitively diagnose NASH, which necessitates the joint presence of steatosis, ballooning and lobular inflammation. Once pathologically confirmed, the severity of NAFLD and NASH is determined using the histologically validated NAS, which grades disease activity on a scale of 0 to 8. The NAS is the sum of the individual scores for steatosis (0 to 3), lobular inflammation (0 to 3), and hepatocellular ballooning (0 to 2) but does not include a score for fibrosis.

Fibrosis staging (F0-F4) relies on the Kleiner classification (F0 = no fibrosis; F1 = perisinusoidal or periportal fibrosis (not both); F2 = both perisinusoidal and periportal fibrosis; F3 = bridging fibrosis; F4 = cirrhosis).

Histological diagnosis remains the gold standard for assessment of NASH and fibrosis. However, given that liver biopsy is associated with risks of pain, bleeding and other morbidity, as well as significant cost, the procedure is not practical for general patient screening. Several non-invasive tools such as clinical risk scores and imaging techniques are increasingly used to assess NASH patients. Clinical risk scores such as the NAFLD fibrosis score, Fibrosis-4 index, the Enhanced Liver Fibrosis score and vibration-controlled transient elastography (“VCTE”), have been validated and are increasingly used. These tools have an excellent negative predictive value and an acceptable positive predictive value for detection of advanced (≥ F3) fibrosis, and are increasingly used in clinical settings. Additionally, evidence is emerging that shows a correlation between reduction in steatosis as measured by magnetic resonance imaging proton density fat fraction (“MRI-PDFF”) and improvement histological changes in the liver. Extensive efforts are also under way to develop non-invasive means to identify patients with NAS ≥ 4 or fibrosis ≥ F2 patients without a need for a liver biopsy. In a recent draft guidance, the FDA encouraged sponsors to identify biochemical or noninvasive imaging biomarkers that, once characterized and agreed by the FDA, could replace liver biopsies for patient selection and efficacy assessment in clinical trials.

We expect that the validation and subsequent adoption of these new tools will result in an increase in the diagnosis and treatment rates for NASH in the future.

Prevalence

The prevalence of NASH has increased significantly in recent decades, paralleling similar trends in the prevalence of obesity, insulin resistance and Type 2 diabetes. Alarmingly, the prevalence of these conditions is expected to increase further in view of the unhealthy nutrition habits, such as consumption of a diet high in fructose, sucrose and saturated fats, and sedentary behavior that characterize modern lifestyle. In the United States, the number of NASH cases is projected to expand from 16.5 million in 2015 (5.1% of the population) to 27 million in 2030. Approximately 20% of the 16.5 million NASH cases in 2015 had F3/F4 fibrosis, a number that is expected to increase to 7.9 million by 2030, which will be approximately 30% of the total NASH population. Similar growth trends for NASH cases are expected in Europe (12.6 million in 2016 to 18.3 million in 2030 within France, Germany, Italy, Spain and the United Kingdom) as well as China (32.6 million in 2016 to 48.3 million in 2030).

Since no approved drugs exist currently, NASH is emerging as a major economic issue. Lifetime costs of all NASH patients in the United States in 2017 was estimated at $223 billion, and the cost of the advanced NASH population was estimated at $95 billion with estimated increase in NASH cases (as mentioned above) further expected to drive costs upwards. Progression of patients along the NASH continuum further adds to costs as mean health care costs (per month) were 32% and 247% higher for patients with compensated cirrhosis ($1,870) and end-stage liver disease ($4,931), respectively, compared to those without cirrhosis ($1,420) and these results were independent of age. The economic burden of NASH is expected to continue to increase, as NASH is anticipated to become the leading cause of liver transplants by 2020 in conjunction with the significant increase in liver transplant costs ($577,000 in 2013 to $812,500 in 2017).

Overview of NASH Treatment Options

There are currently no approved therapies for the treatment of NASH. We believe four key attributes are essential for successful NASH therapies: (1) robust efficacy with respect to liver pathologies; (2) ability to address underlying co-morbidities associated with the disease; (3) limited tolerability issues at effective doses; and (4) patient convenience. Figure 4 below summarizes the primary interventional and therapeutic approaches to NASH that are in existence or under development and their key advantages and limitations.

Figure 4: Primary Interventional and Therapeutic Approaches to NASH

Approach	Advantages	Limitations
Diet and exercise	▪ Reduction in continuing injury to the liver allowing liver to regenerate ▪ Inexpensive and widely available	▪ Poor adherence
Farnesoid X receptor (FXR) agonism	▪ Statistically significant but modest reduction in liver fibrosis ▪ Liver fat reduction with some agents	▪ Increase in LDL-C and pruritus with some agents ▪ Limited impact on NASH resolution by histology
Peroxisome proliferator-activated receptor (PPAR) agonism	▪ Improvement in glycemic control with some agents ▪ Anti-inflammatory ▪ Reduction in triglycerides and liver fat with some agents	▪ Weight gain with certain agents ▪ Safety issues with certain agents (cancer, heart failure, edema, interface hepatitis) and renal adverse events ▪ No effect on liver fat with certain agents
Thyroid receptor-ß (THR-ß) agonism	▪ Reduction in LDL-C and triglycerides ▪ Reduction in liver fat	▪ Potential for drug-drug interactions ▪ Potential risk of hypothyroidism ▪ Questionable effect on fibrosis
Acetyl-CoA (ACC) inhibition	▪ Reduction in DNL from inhibition	▪ Increase in triglycerides, risk of thrombocytopenia
Fibroblast growth factors (FGFs)	▪ Reduction in liver fat and fibrosis ▪ Improvements in lipid parameters with certain agents	▪ FGF19 is associated with increases in LDL-C; impact on HDL and glucose unclear ▪ Daily injections with some agents likely to be poorly received by patients ▪ Native FGF21 is rapidly broken down by the body and is difficult to formulate in solution
GLP1	▪ Reduction in body weight ▪ Well-established glycemic control agent	▪ No impact on lipid parameters ▪ Injectable formulation in testing for NASH has burdensome dosing regime ▪ Questionable impact on fibrosis and liver fat reduction

We believe that the market for NASH treatments will evolve to be similar to the multi-billion dollar markets for diabetes and dyslipidemia treatments and has the potential to support multiple successful commercial products across different therapeutic classes as well as within the same class. Further, we believe potent injectable therapies have the potential to be a preferred treatment option for some patient populations.

Our Solution

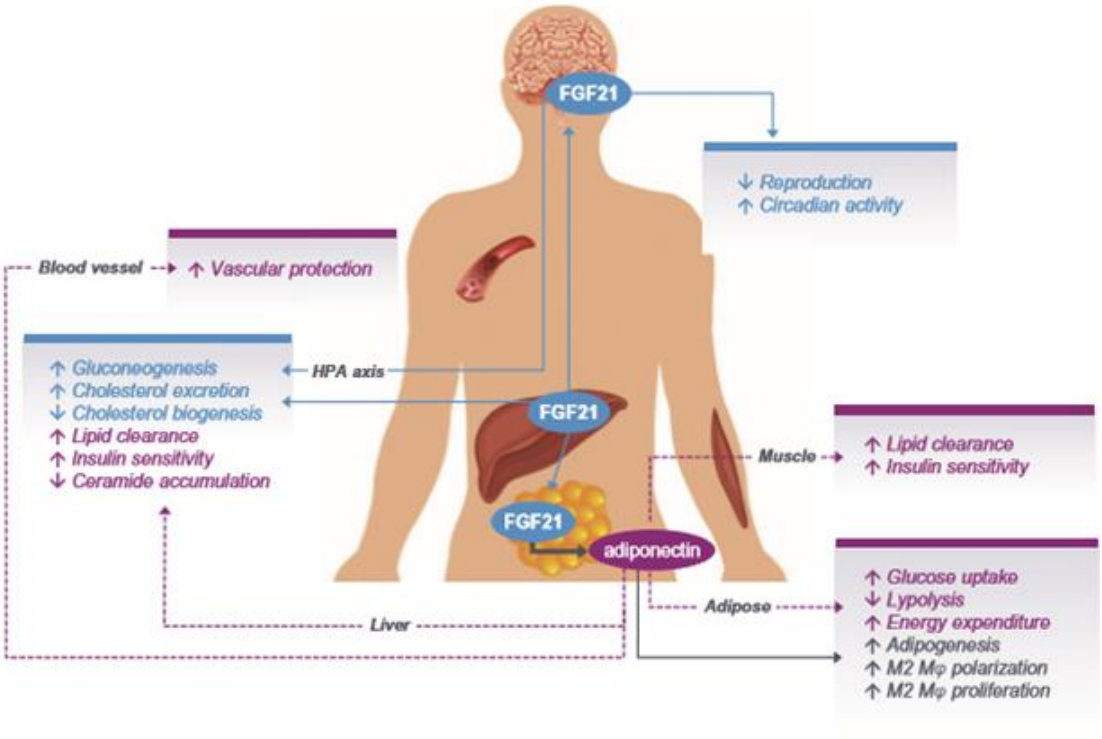
Summary

We are developing BIO89-100, a specifically engineered glycoPEGylated analog of FGF21, for the treatment of NASH and other liver and cardio-metabolic indications. FGF21 is an endogenous metabolic hormone that is naturally found as a monomeric, non-glycosylated protein and is known to play a key role in regulating energy expenditure, and glucose and lipid metabolism. FGF21 has been clinically shown to reduce steatosis in the liver. It is also thought to exert effects on liver fibrosis by improving metabolic regulation, which reduces ongoing liver injury thus giving the liver time to heal. FGF21 also generates an on-target effect to increase adiponectin, a hormone released from adipose tissue that, among other functions, can suppress development and progression of hepatic fibrosis. Given the relevant and broad-based effects of FGF21, we believe it is a compelling pharmaceutical target for treating NASH, which may offer benefits and/or address the limitations relative to the therapeutic approaches described in Figure 4 above. We believe FGF21 analogs such as ours have the potential to be the mainstay of therapies for NASH because they can address liver pathologies and the underlying metabolic dysregulation which result in NASH progression. However, FGF21 in its native form is not suitable as a pharmacological product given it is rapidly broken down by the body and it is unstable in soluble formulation. BIO89-100 is specifically engineered to overcome these challenges while maintaining the efficacious properties of the endogenous molecule. We believe BIO89-100 may be a differentiated FGF21 therapy based on its robust and durable biological effects and a favorable tolerability profile, as well its potential for a longer dosing interval. We are currently evaluating BIO89-100 in a POC Phase 1b/2a clinical trial in patients with NASH or patients with NAFLD and high risk of NASH.

FGF21 Overview

Fibroblast growth factors (“FGFs”), including FGF21 and FGF19, are a large family of cell-signaling proteins involved in the regulation of many processes within the body. FGF21 is an endogenous metabolic hormone that regulates energy homeostasis, glucose-lipid-protein metabolism and insulin sensitivity, and modulates the pathways that mitigate against intracellular stress. FGF21 is secreted primarily by the liver but is also secreted by the white adipose tissue (“WAT”), skeletal muscle and the pancreas. FGF21 exerts its biological benefits through the activation of three fibroblast growth factor receptors (“FGFRs”), FGFR1c, FGFR2c and FGFR3c, and requires co-activation of the transmembrane protein cofactor beta Klotho (“ß-Klotho”). FGF21 is not believed to activate FGFR4, which has been associated with adverse effects. FGF21 can act directly or indirectly on target organs by mediating downstream regulators, such as adiponectin, and upstream regulators that induce FGF21, such as nutritional stress or transcription factors. Figure 5 below shows effects of FGF21 on the body.

Figure 5: Biological Effects of FGF21



Reducing Liver Steatosis by Improving Lipid Handling and Insulin Sensitivity

FGF21 has been clinically shown to reduce liver steatosis. FGF21 reduces liver steatosis by (1) increasing fatty acid oxidation in the liver, (2) reducing the deposition of free fatty acids from peripheral tissue to the liver and (3) reducing DNL in the liver. FGF21 exerts its systemic effects by reducing the serum levels of lipids (e.g., triglycerides, LDL cholesterol) and increasing insulin sensitivity. Increasing insulin sensitivity reduces lipolysis and can also reduce serum levels of lipids. In particular, FGF21 has been demonstrated to reduce liver fat in patients with NASH and has also shown beneficial effects in obese diabetic patients on both serum levels of lipids and insulin resistance.

Improving Liver Inflammation and Fibrosis

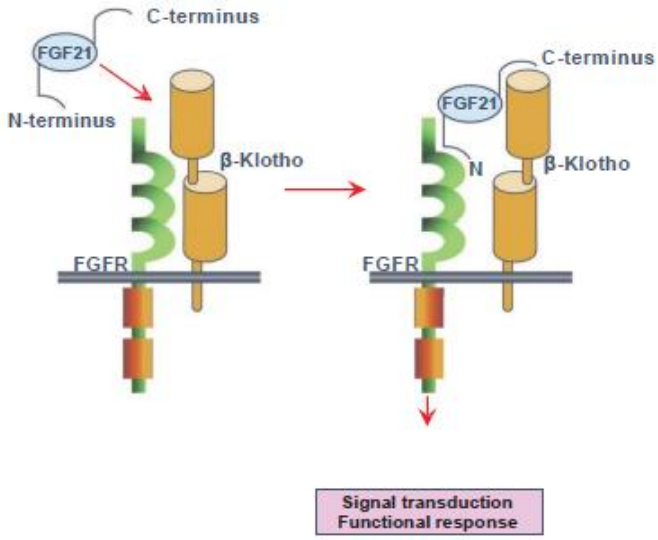
FGF21 is believed to reduce liver fibrosis, the pathological change mostly clearly linked to liver-related morbidity in NASH patients via two potential pathways. One pathway is through the metabolic benefits of FGF21 described above. Long-term improvements in metabolic regulation reduce the ongoing liver injury that drives fibrosis and thus allows the liver time to heal. The other pathway is a direct anti-fibrotic effect mediated via adiponectin, an adipokine that is upregulated by FGF21. Increased adiponectin downregulates the hepatic stellate cells that are activated upon hepatic injury and responsible for collagen deposition and subsequent fibrosis.

FGF21 Signaling

As noted above, FGF21 exerts its biological benefits through the co-activation of FGFRs and ß-Klotho. FGFRs are expressed widely throughout the body whereas ß-Klotho is primarily expressed in metabolic tissues such as adipose tissue, liver, and pancreas, thereby providing organ specificity to FGF21.

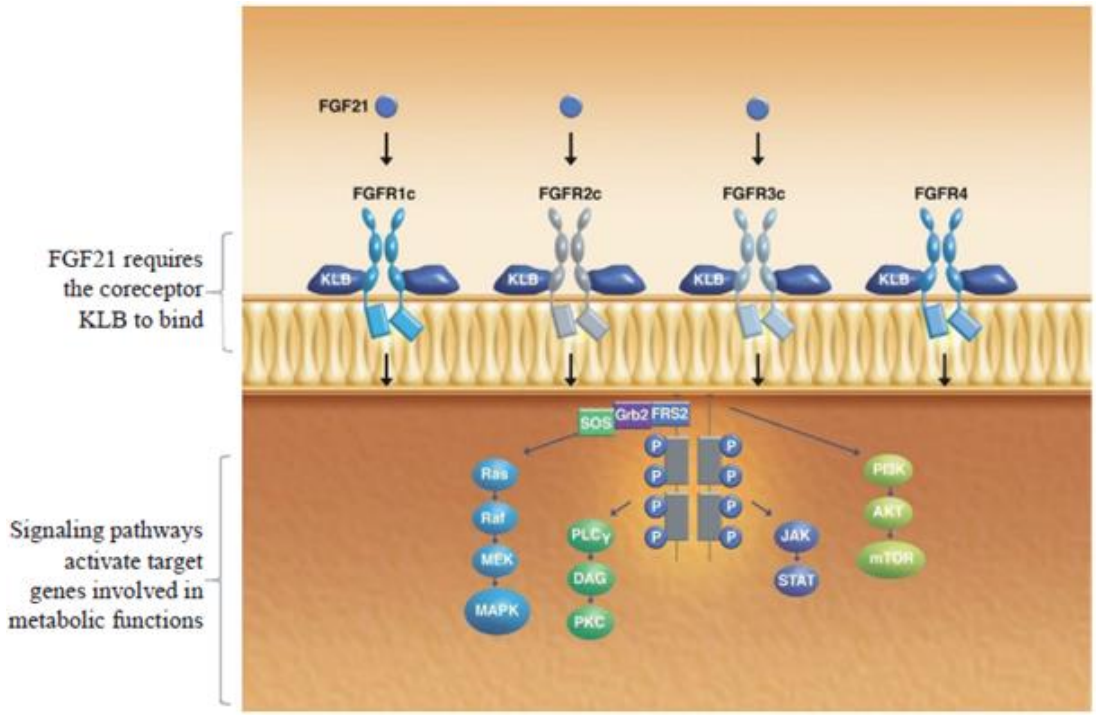
As illustrated in Figure 6 below, the binding of FGF21 is a two-step process. The C-terminus of FGF21 initially binds to ß-Klotho enabling the N-terminus to form an expanded complex with one of the FGFRs. Once the co-receptor complex has formed with ß-Klotho and one of the FGFRs, a series of intracellular signaling cascades is initiated. These signaling cascades enable FGF21 to exert its biological functions.

Figure 6: FGF21's two-step receptor binding with ß-Klotho and FGFRs



FGF21 activates three specific FGFRs (FGFR1c, FGFR2c and FGFR3c), which based on nonclinical studies and clinical trials, appear to be responsible for mediating the desired therapeutic actions of FGF21 in NASH. FGF19 activates these receptors and acts upon another FGFR known as FGFR4. Activation of FGFR4 results in an increase in LDL cholesterol and has been implicated in the etiology or progression of HCC. The activation and downstream signaling pathways of FGF21 are shown in Figure 7 below.

Figure 7: FGF21 Receptor Activation



Overcoming the Challenges of Developing FGF21 as a Pharmaceutical Product

While the observed pharmacological effects of recombinant human FGF21 in preclinical disease models clearly highlight its therapeutic potential, FGF21 in its native form is not suitable for commercialization for two key reasons:

- ***Native FGF21 is rapidly broken down in the bloodstream and cleared through the* kidneys.** The native form of FGF21 is a 19.4 kDa protein with a half-life estimated to be less than two hours. Reducing renal clearance and protecting both ends of the protein from proteolysis remains key to extending half-life and thereby extending the duration of its effect. If the N-terminus is not intact, signaling activity of FGF21 is significantly reduced. However, if the C-terminus is not intact, FGF21's ability to bind with ß-Klotho is impaired, thereby rendering it inactive.
- **Native FGF21 is unstable and has a tendency to aggregate in solution.** Hence, it is operationally challenging to develop a stable liquid formulation at high concentration with low viscosity, which is required to achieve good bioavailability via subcutaneous injection.

Clinical Validation of FGF21 and FGF class of drugs

We believe FGF21 has the potential to be the mainstay monotherapy for NASH because it addresses multiple facets of the disease. Specifically, it has the potential to reduce steatosis, improve fibrosis and importantly, impact the metabolic dysregulation which continues to promote disease progression. The potential for FGF21 analogs in the treatment for NASH has been demonstrated by clinical trial data with pegbelfermin, a pegylated form of FGF21. In a third-party Phase 1b study, pegbelfermin was observed to result in reductions in triglycerides, LDL-C and HDL. In addition, a third-party Phase 2a study conducted in patients with biopsy-proven NASH, pegbelfermin showed a significant reduction in absolute hepatic fat fraction measured by MRI-PDFF, a significant increase in adiponectin concentration, a decrease in mean liver stiffness and a significant decrease in concentration of PRO-C3, a biomarker of fibrosis. Clinical outcomes were better when dosed as a daily injection versus a weekly injection. The compound was deemed generally well tolerated, although a higher frequency of gastrointestinal adverse events was reported in treated patients versus placebo.

A second compound, selectively activating the FGFR1c and its co-receptor ß-Klotho, reported reductions in liver fat content and improvements in metabolic parameters in a study in NAFLD patients.

In addition, the potential for FGF19 analogs in the treatment for NASH has been demonstrated with aldafermin, an engineered version of the human hormone FGF19. In a third-party Phase 2 study conducted in patients with biopsy-confirmed NASH, aldafermin showed a significant reduction in absolute liver fat content measured by MRI-PDFF and a statistically significant improvement in fibrosis and NASH resolution relative to placebo after 24 weeks of treatment. FGF19 and FGF21 share key commonalities in their mechanism of action and activate many of the same FGF receptors in the body. However, a key difference is that FGF21 is not believed to activate the FGFR4 receptor while FGF19 does activate this receptor. As a result of the activation of FGFR4, LDL levels rise and aldafermin treatment resulted in significant increase in LDL levels in the clinical trial necessitating protocol-driven administration of statins. Additionally, aldafermin was dosed as a once daily injection in the trial.

BIO89-100

Overview

We are developing BIO89-100, a specifically engineered glycoPEGylated analog of FGF21, for the treatment of NASH with fibrosis and other cardio-metabolic indications. BIO89-100 has successfully completed a Phase 1a study, and we are currently evaluating BIO89-100 in a POC Phase 1b/2a clinical trial in patients with NASH or NAFLD with a high risk of NASH. BIO89-100 has been specifically engineered to: (1) protect against proteolysis and reduce renal clearance, (2) have an extended half-life, (3) minimize susceptibility to aggregate in solution and (4) optimize its potency, enabling the potential use of lower dosage/doses. Additionally, we believe that BIO89-100 may enhance binding affinity for ß-Klotho, by altering the conformation of the C-terminus which could have a positive impact on efficacy.

Primary Structure and Protein Engineering of BIO89-100

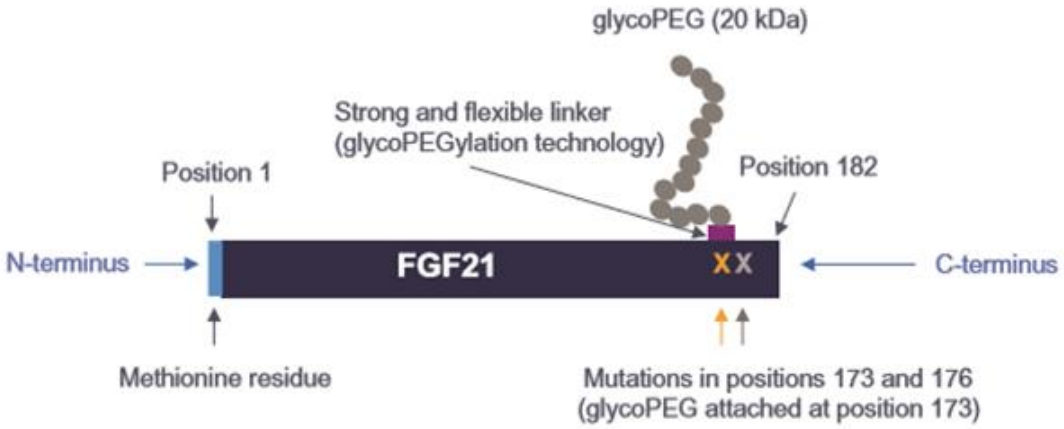
BIO89-100 has been optimally constructed with two mutations via substitutions with natural amino acids at site-specific positions (173 and 176) toward the C-terminus end of the hormone. The mutations were incorporated into the FGF21 sequence after existing proline to create a consensus sequence for glycosylation. Subsequently, the glycosyl linker and a single 20 kDa glycoPEG moiety were enzymatically introduced at the O-linked glycosylation consensus site (position 173) via the proprietary glycoPEGylation technology. Our glycoPEG moiety is an activated form of the PEG molecule with the use of Sialic Acid, CMP-SA-PEG. The proximity of the mutations ensures consistent and efficient attachment of the glycoPEG moiety.

BIO89-100 has two modified natural amino acid residues:

- S173T: Serine modified to Threonine at position 173; and
- R176A: Arginine modified to Alanine at position 176.

In addition, a Methionine residue was introduced at the N-terminus which acts as the translation initiation signal. A single 20 kDa linear glycoPEG moiety is attached to the Threonine in position 173 via the proprietary glycoPEGylation technology. Figure 8 below shows the structure of BIO89-100.

Figure 8: Structure of BIO89-100



The increase in the size of the molecule from 19.4 kDa to 40 kDa together with the site-specific mutations adjacent to the primary cleavage site of FGF21 (by the FAP enzyme between positions 171 and 172 on the native amino acid chain, which would be represented by positions 172 and 173 in our molecule starting with Methionine in position 1) are designed to prolong the half-life of the molecule. Additionally, we believe that the use of glycoPEGylation technology produces a comparatively stronger and more flexible structure, which aids in the development of a stable formulation. PEGylation technology has been used successfully in many pharmaceutical products including products that have been marketed for more than 10 years.

BIO89-100 uses a proprietary glycoPEGylation technology that has been previously validated by a third party, as this technology is incorporated in another pharmaceutical product (Lonquex® by Teva) that has received regulatory approval and is currently commercialized in the European Union.

The Development and Selection of BIO89-100

The discovery program that led to the selection of BIO89-100 was directed towards achieving an optimal PK and efficacy profile. It has been shown that the in vivo half-life of FGF21 can be extended by covalently linking a single glycoPEG moiety to the molecule. We performed extensive screening of FGF21 analogs with mutations at different positions including close to the N-terminus, as well as different glycoPEGylations to select an optimized molecule based on its potency, PK and in-vivo efficacy.

Stage I—Optimizing Selection of Mutation Sites—In Vitro Potency Testing

Mutations were inserted at different sites for both non-PEGylated FGF21 analogs and corresponding glycoPEGylated analogs and screened in a cell-based potency assay to select analogs that did not lose potency relative to the native hormone. Amongst the multiple glycoPEGylated analogs tested, only mutations at sites towards either N-terminus or C-terminus showed potency comparable to that of native FGF21 hormone and were selected for further development.

Stage II—Optimizing for glycoPEG (20 kDa vs 30 kDa)—In Vitro Potency Testing

Analogs selected in Stage I were prepared with either a 20 kDa or a 30 kDa glycoPEG moiety and tested for potency in mouse adipocytes (3T3-L1) and human embryonic kidney (HEK-293) cell lines. Minimal differences in potencies were observed between the 20 kDa and 30 kDa glycoPEGylated analogs. However, only the glycoPEGylated analogs that had mutations and a glycoPEG attachment at the C-terminus, as distinct from those with mutations at the N-terminus, maintained their potency in both mouse and human cell lines. These analogs were selected for future development.

Stage III—Optimizing for PK Properties and Efficacy—In Vivo Testing

Selected analogs from Stage II with either a 20 kDa or a 30 kDa glycoPEG moiety, were chosen for in vivo testing in a diabetic mouse model. In addition to PK, changes from baseline in glucose, triglycerides and insulin were measured. The data showed that the circulating half-life of the glycoPEGylated analogs for both glycoPEG sizes was extended (range 15 to 30 hours) as compared to native FGF21 (2 hours). As expected, all analogs were observed to cause a reduction in blood glucose levels. However, the 20 kDa glycoPEGylated analogs were observed to outperform the 30 kDa analogs by improving triglycerides at lower doses and across broader dose ranges. BIO89-100 resulted in the greatest reduction of insulin and was selected as the candidate for clinical development.

In summary, the mutations made to the native FGF21 molecule and the addition of the 20 kDA glycoPEG moiety via the use of the glycoPEGylation technology were observed to significantly improve the PK properties of the molecule while retaining the therapeutic benefits. We believe that BIO89-100 is a well-balanced molecule with a unique profile, which has the potential to have therapeutic benefits in NASH and cardio-metabolic diseases. Figure 9 below sets forth what we believe are the key features and potential benefits of BIO89-100:

Figure 9: Summary of BIO89-100 Attributes and Benefits

Features	Description	Potential Benefit
Use of PEG (via glycoPEGylation)	▪ Increases protein size and hydrodynamic volume that reduces renal filtration ▪ Prevents degradation by endocytosis and proteolytic enzymes	▪ Prolongs half-life
	▪ Protects antigenic sites present on the protein surface (i.e. antigenic epitopes)	▪ Reduces immunogenicity
	▪ Steric repulsion between the PEGylated surfaces increases water solubility and reduces aggregates	▪ Results in more stable formulation
Site-Specific Mutations	▪ Mutation at position 173 is immediately adjacent to the primary cleavage (FAP enzyme) site of FGF21	▪ Prolongs half-life
GlycoPEGylation Technology	▪ Allows site specific linkage (glycoPEG moiety to position 173) ▪ Proximity of the glycoPEG moiety to the C-terminus induces conformational changes to the molecule	▪ Retains potency against receptor to improve efficacy
	▪ Provides a strong and flexible glycosyl bond that helps the glycoPEG moiety remain intact, further reducing degradation	▪ Further enhances half-life

Therapeutic Potential of BIO89-100 Supported by Preclinical Animal Models of NASH, Diabetes and Obesity

BIO89-100 was evaluated in multiple distinct animal models of NASH, diabetes and obesity, including non-human primate studies. In each of these studies, consistent and significant beneficial effects were observed across a range of endpoints, specifically, robust improvements in lipid handling, glycemic control and insulin resistance as well as significant improvements in hepatic steatosis, injury and fibrosis. We believe these results demonstrate the potential of BIO89-100 to simultaneously address the multiple drivers of NASH pathogenesis. The histological endpoints, NAS and fibrosis score, mirror the endpoints we expect to assess in our clinical development. In addition, treatment with BIO89-100 in animal models was observed to result in consistent reductions in body weight.

BIO89-100 has been evaluated in three animal models of direct relevance to NASH. These included: (1) Stelic Animal Model ("STAM"), (2) Diet-induced NASH ("DIN") model and (3) spontaneous diabetic obese cynomolgus monkey model. Additional studies done in diabetes mouse model and diet induced obesity mouse model showed benefits in key markers of relevance in NASH.

A wide range of doses were tested in these studies as well as weekly and once every two week dosing regimen was tested in a cynomolgus monkey study. The key outcomes of these studies are summarized in Figure 10 below.

Figure 10: Summary of NASH Pharmacology Studies

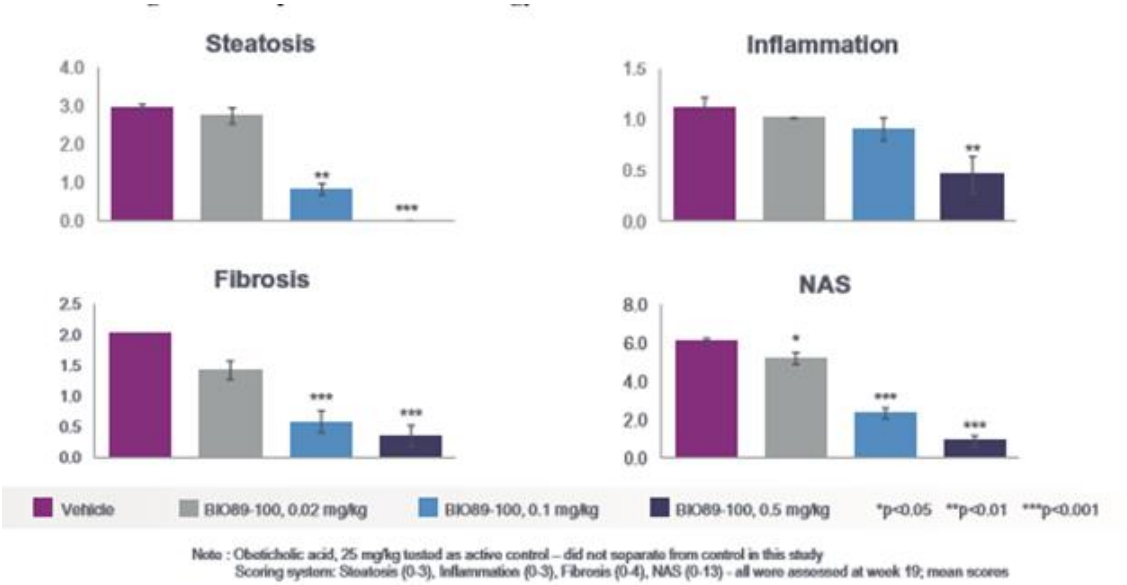
Preclinical pharmacology study with BIO89-100	Improved Insulin Sensitivity	Improved Lipid Handling	Reduced Hepatocyte Injury	Reduced Fibrosis
STAM mouse model	✓	✓	✓	*
DIN mouse model I (10 weeks)	✓	✓	✓	✓
DIN mouse model II (19 weeks)	✓	✓	✓	✓
Diabetic obese cynomolgus monkey study 1 (8 weeks; weekly dosing)	✓	✓	✓	Not evaluated
Diabetic obese cynomolgus monkey study 2 (4 weeks; QW or Q2W dosing)	✓	✓	✓	Not evaluated

Legend:
✓ Statistically significant benefit observed
* Improvement observed, but did not achieve statistical significance.

Results of DIN Mouse Studies

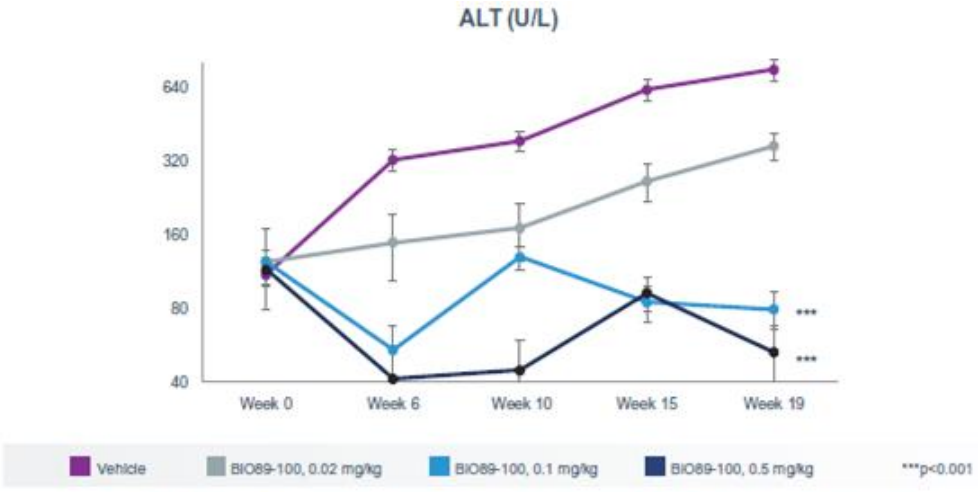
Two pharmacology studies were conducted in a DIN mouse model. In the first study of 40 mice (10 per treatment group), the animals received BIO89-100 via a subcutaneous injection at 0.5 and 2 mg/kg every 3 days for 10 weeks, and a detailed assessment of liver parameters was performed to evaluate the effectiveness of the dosing regimen. Both doses of BIO89-100 were observed to reduce the total NAS significantly based on histological evaluation and improved measures with respect to both lipid handling and insulin sensitivity. In addition, expression of hepatic genes involved in inflammation and fibrosis were significantly reduced following administration of BIO89-100. In the second DIN mouse study of 50 mice (10 per treatment group), lower dose levels of BIO89-100 were tested (0.02, 0.1 and 0.5 mg/kg every 3 days) but the treatment duration was longer at 19 weeks. In this study too, BIO89-100 was observed to result in significant reductions in the liver damage induced by the diet in a dose-dependent manner. Specifically, treatment with BIO89-100 was observed to result in a significant mean reduction of the histological markers of NASH (Figure 11), as well as a reduction in the marker of hepatic injury (alanine amino transaminase ("ALT")) (Figure 12), in liver lipids (Figure 13), and in inflammatory and fibrotic markers (Figure 14), each in a dose dependent manner compared to vehicle treatment. In addition to the beneficial effects on the liver, treatment with BIO89-100 demonstrated significant improvements in glycemic control and weight loss. As NAS and measures of fibrosis are histological endpoints for the assessment of NASH in clinical studies, we believe that the observations in the STAM and DIN mouse models suggest that BIO89-100 is a compelling candidate for the treatment of NASH.

Figure 11: Improvement in Histology with BIO89-100 in a DIN Mouse Model



Note : Obeticholic acid, 25 mg/kg tested as active control – did not separate from control in this study
Scoring system: Steatosis (0-3), Inflammation (0-3), Fibrosis (0-4), NAS (0-13) - all were assessed at week 19; mean scores

Figure 12: Changes in ALT with BIO89-100 in a DIN Mouse Model



Note: Obeticholic acid, 25 mg/kg tested as active control – did not separate from control in this study; data presented are mean values

Figure 13: Reduction in Liver Lipids with BIO89-100 in a DIN Mouse Model

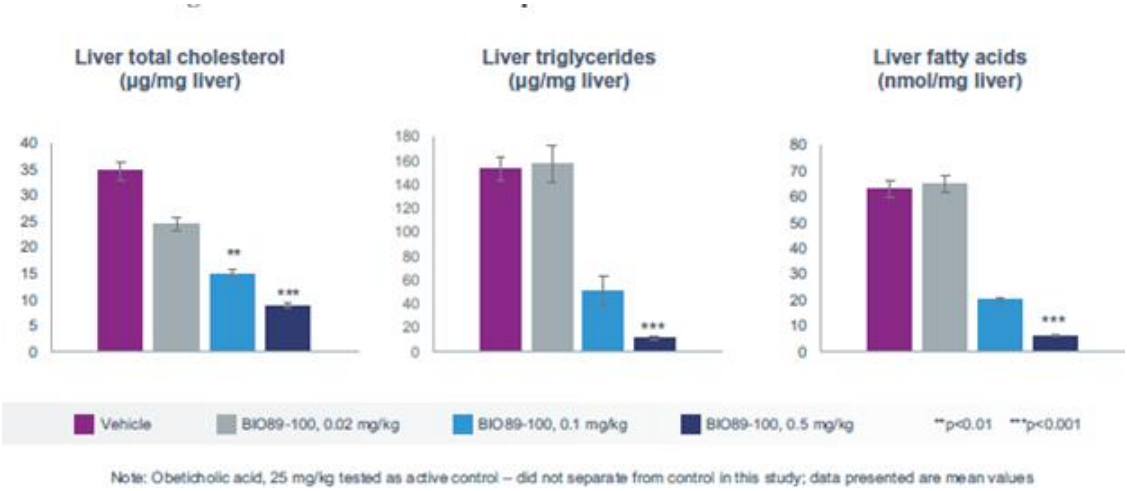
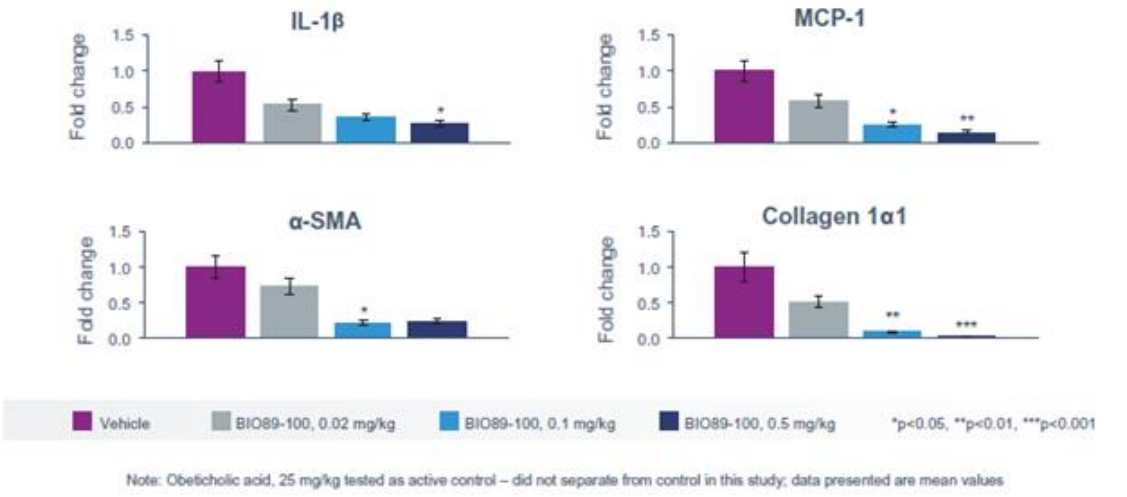


Figure 14: Changes in Inflammatory and Fibrotic Markers with BIO89-100 in a DIN Mouse Model



Results of Spontaneously Diabetic Obese Cynomolgus Monkey Studies

BIO89-100 efficacy was evaluated in 24 spontaneously diabetic obese cynomolgus monkeys (six per treatment group) after multiple subcutaneous doses. In the first study, BIO89-100 was administered at doses of 0.1, 0.3 and 1 mg/kg once per week for 8 weeks followed by a 6-week washout phase. Administration of BIO89-100 showed significant effects on triglycerides at all doses tested, with a highly robust 78% reduction observed at the highest dose level of 1 mg/kg/week (Figure 15). Statistically significant mean reductions were observed in total cholesterol (Figure 16), glucose (Figure 17), insulin, glycated hemoglobin (HbA1c) and ALT (Figure 18), along with improvement in oral glucose test results.

Figure 15: Changes in Triglycerides with BIO89-100 in Diabetic Monkey Study 1

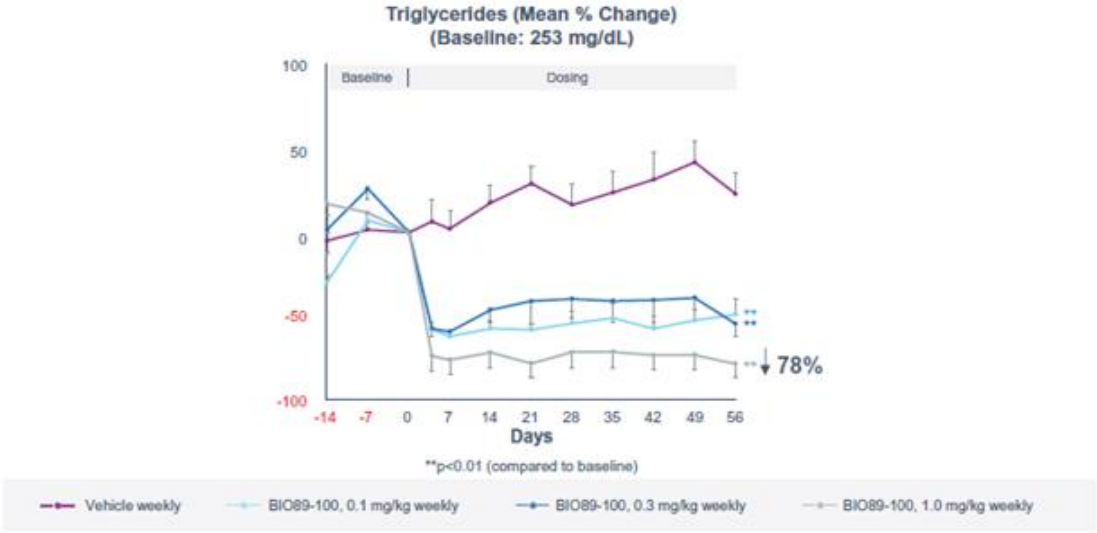


Figure 16: Changes in Total Cholesterol with BIO89-100 in Diabetic Monkey Study 1

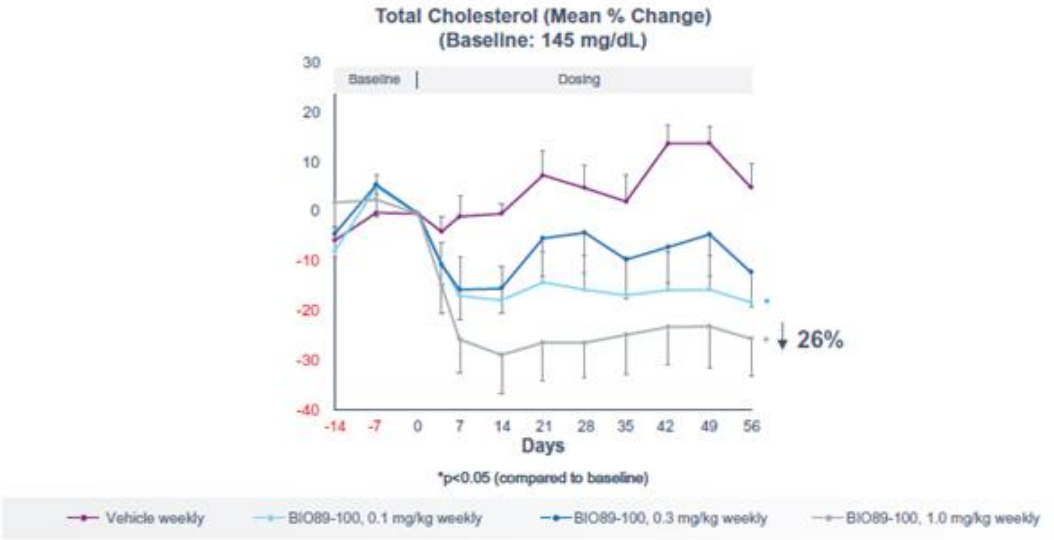


Figure 17: Changes in Blood Glucose with BIO89-100 in Diabetic Monkey Study 1

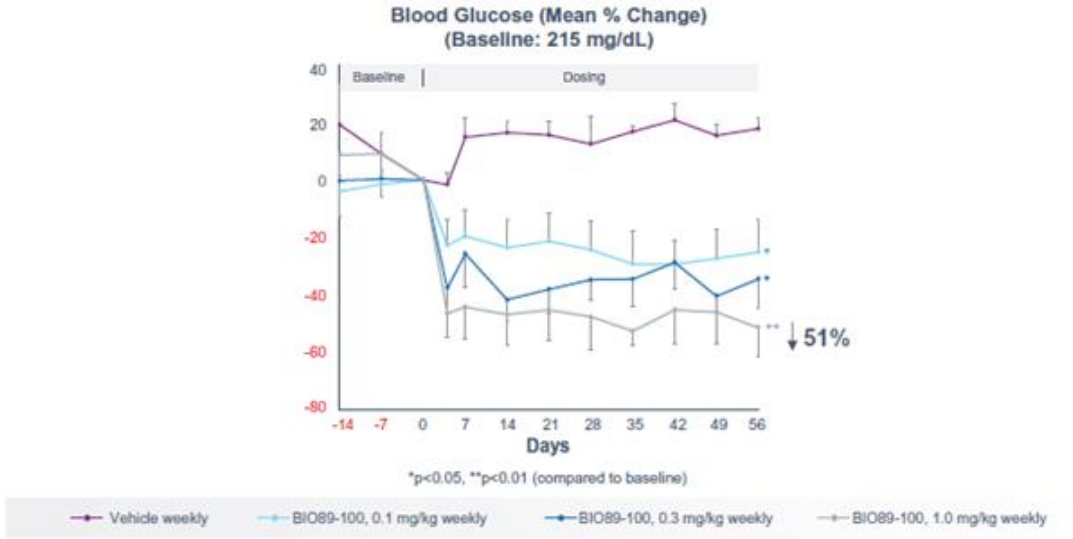
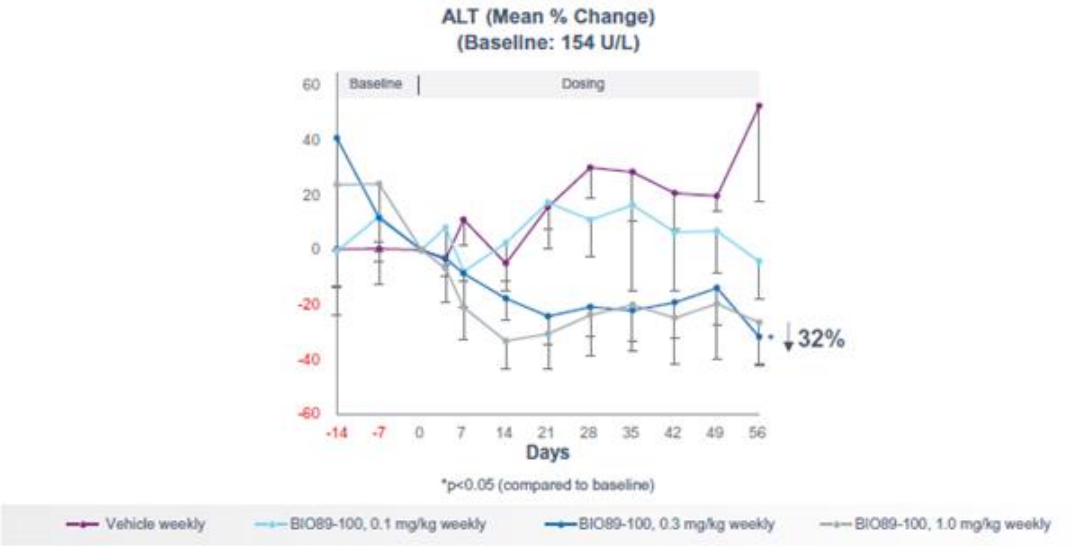


Figure 18: Changes in ALT with BIO89-100 in Diabetic Monkey Study 1



In a second multiple-dose study in 24 spontaneously diabetic obese cynomolgus monkeys (six per treatment group), BIO89-100 was administered for 4 weeks at 1 mg/kg once weekly or 1 or 2 mg/kg given once every 2 weeks. A rapid and dramatic reduction in triglycerides (Figure 21), up to 76%, was observed with BIO89-100. Statistically significant mean reductions were also observed in body weight (Figure 19), HbA1c (Figure 20), glucose, and insulin, along with increased adiponectin levels (Figure 22) and improvement in oral glucose test results in all BIO89-100-treated groups (both once weekly and every 2 weeks) in comparison to the vehicle group. The robust effect on body weight and HbA1c over the 4-week treatment period were particularly unexpected. The PD effects were relatively similar across all three dosing groups suggesting that once every two weeks could be a viable clinical dosing strategy. BIO89-100 was also assessed in a study of sweetness preference in six obese cynomolgus monkeys. Using a two-bottle sweetness preference test, monkeys given BIO89-100 at 1 mg/kg by subcutaneous injection every week for three weeks demonstrated a substantial reduction in sweetness preference and improvements in certain lipid parameters compared to monkeys given vehicle treatment.

Figure 19: Changes in Body Weight with BIO89-100 in Diabetic Monkey Study 2

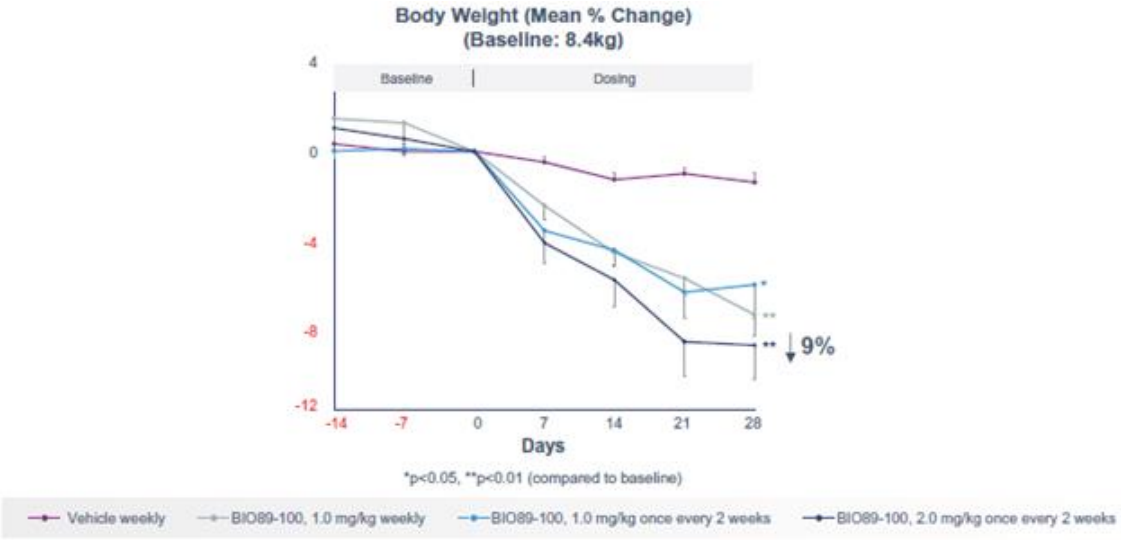


Figure 20: Changes in HbA1c with BIO89-100 in Diabetic Monkey Study 2

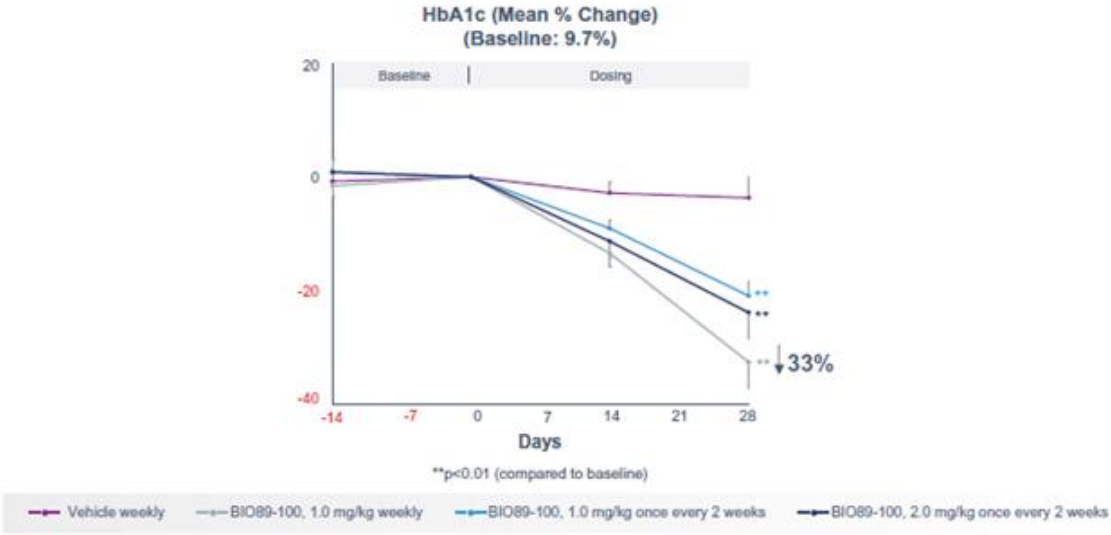


Figure 21: Changes in Triglycerides with BIO89-100 in Diabetic Monkey Study 2

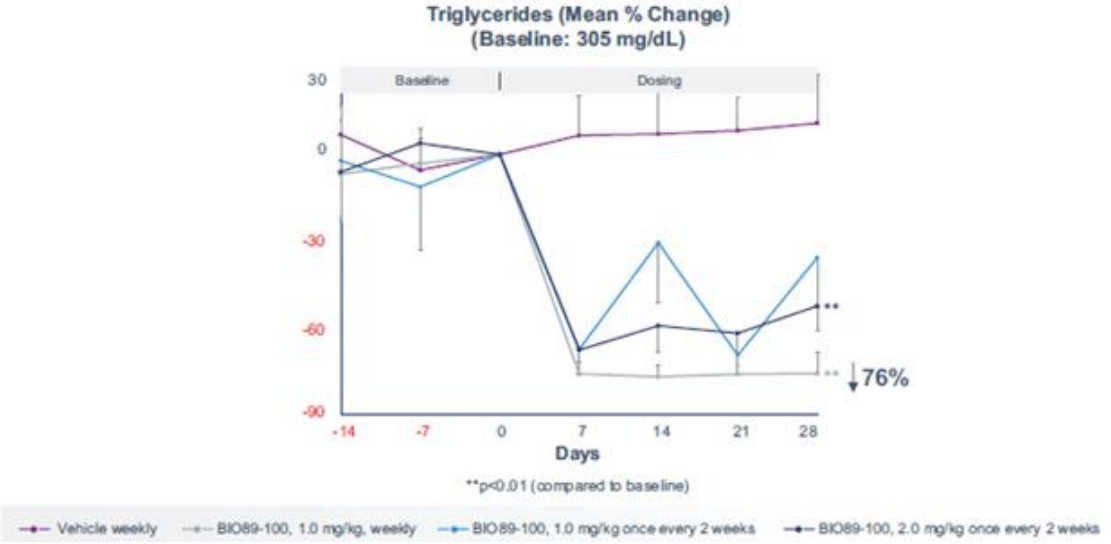
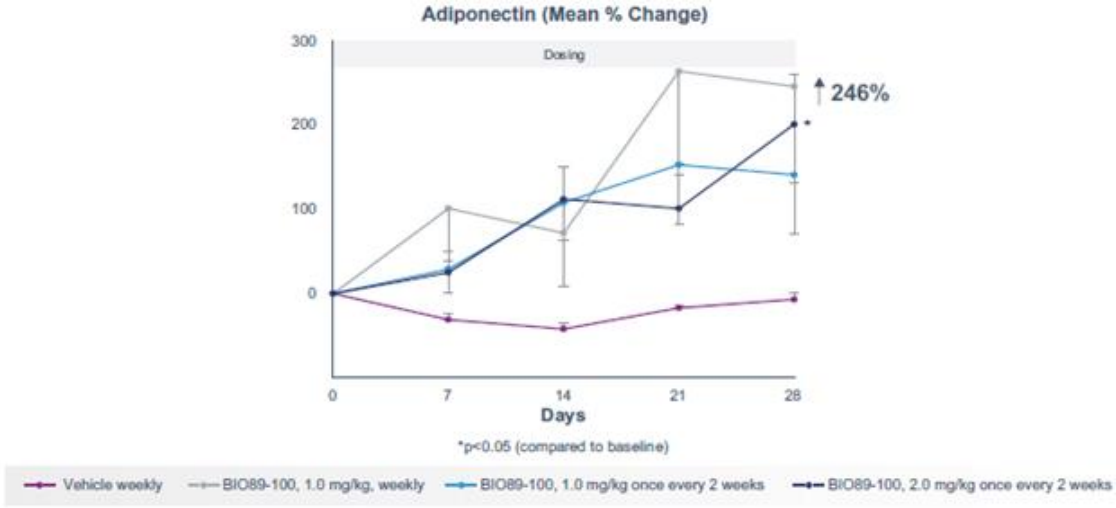


Figure 22: Changes in Adiponectin with BIO89-100 in Diabetic Monkey Study 2



We believe the PD effects observed in the animal studies suggest that BIO89-100 is a potent molecule that may address the key pathways in NASH by (1) improving lipid handling and resultant steatosis, (2) improving insulin resistance, (3) reducing hepatocyte injury and inflammation and (4) improving fibrosis. Additionally, the data from the cynomolgus monkey studies suggest that the molecule may be amenable to an extended dosing interval.

BIO89-100 Clinical Development

We are developing BIO89-100 for the indication of NASH with fibrosis. In our randomized, double-blind, placebo-controlled, Phase 1a, first-in-human, SAD clinical trial of BIO89-100 of 58 healthy volunteers, 43 healthy volunteers received BIO89-100 with a half-life of 55 to 100 hours and 15 received placebo treatment. In this SAD study, BIO89-100 was well tolerated, with all treatment related adverse events reported as mild; there were no serious adverse events reported. At single doses of 9.1 mg and higher, we observed significant improvements in key lipid parameters measured at Day 8 and Day 15 after dosing on Day 1. The mean changes versus baseline include reductions in triglycerides (up to 51%) and LDL-C (up to 37%) and increase in HDL-C (up to 36%) despite the baseline values being in the normal range. As compared to placebo treatment, these mean changes were all statistically significant ($p < 0.001$). BIO89-100 demonstrated rapid (starting from Day 2), sustained and durable improvements on lipid parameters for two weeks or more after single dose administration. We believe this duration of effect further supports the possibility of an extended dosing interval, as observed in our preclinical studies.

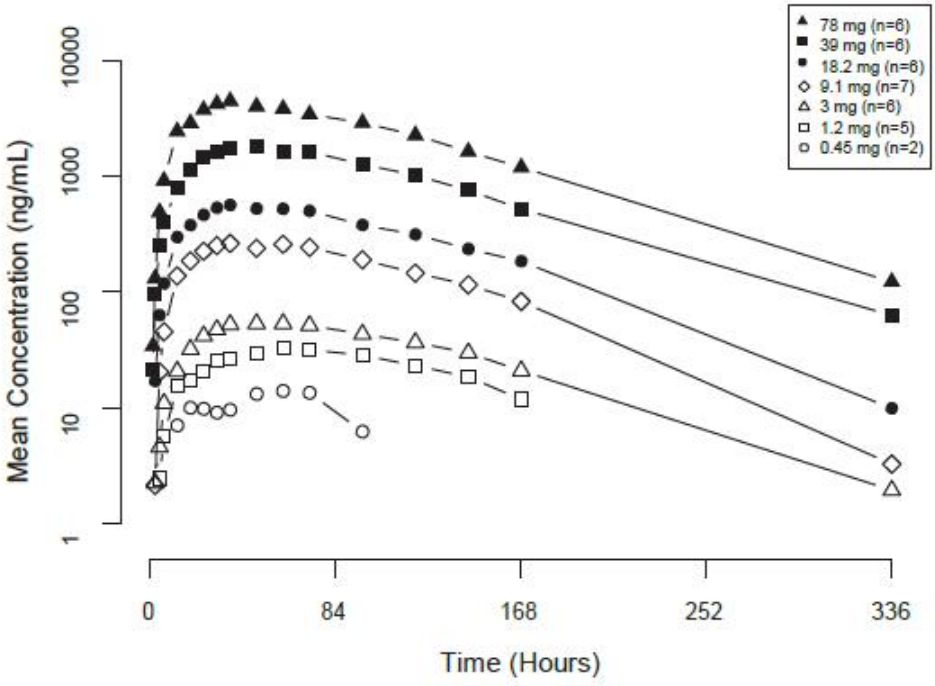
Phase 1a Clinical Trial of Single Dose of BIO89-100 in Healthy Volunteers

We conducted a Phase 1a clinical trial to evaluate the safety, tolerability and PK of BIO89-100 in healthy volunteers. We enrolled a total of 58 healthy volunteers into one of seven cohorts and randomized to receive a single dose of BIO89-100 or a placebo. Forty-three healthy subjects received BIO89-100 at the following doses: 0.45 mg, 1.2 mg, 3 mg, 9.1 mg, 18.2 mg, 39 mg and 78 mg.

BIO89-100 Exhibited Generally Linear, Dose-proportional PK

The PK profile of BIO89-100 was generally dose-proportional or slightly more than dose-proportional with T1/2 range from approximately 55 to 100 hours. As shown in Figure 23 below, the observed median time of maximum serum concentration ranged from 36 to 60 hours.

Figure 23: Single-dose PK of BIO89-100



Our Phase 1a clinical trial enrolled healthy volunteers with a mean (SD) age and BMI of 39.3 (9.7) years and 26.7 (3.1) kg/m2 respectively, with laboratory parameters in the normal range at baseline (mean values: TG 94.0 mg/dL; LDL 124.1 mg/dL; HDL 47.7 mg/dL). Even in this healthy study population, after a single dose administration of BIO89-100 at doses 9.1 mg and higher, robust and durable PD effects were observed across key lipid parameters, including triglycerides (Figures 24 and 25), LDL (Figure 26) and HDL (Figure 27), over two weeks. The changes in lipids parameters started from Day 2 with maximal effects typically observed at Day 8 or Day 15. The effect on lipid parameters was generally dose-dependent, with single doses of BIO89-100 at 9.1 mg and higher, demonstrating significant improvements versus baseline in key lipid parameters measured at Day 8 and Day 15 following dosing. The BIO89-100 effects appeared to plateau at 39 mg with minimal additional effect observed in 78 mg. BIO89-100 also led to increases in mean adiponectin levels (up to 146% relative to baseline) when measured at Day 8 and Day 29.

Figure 24: Changes in Triglycerides after Single Dose of BIO89-100

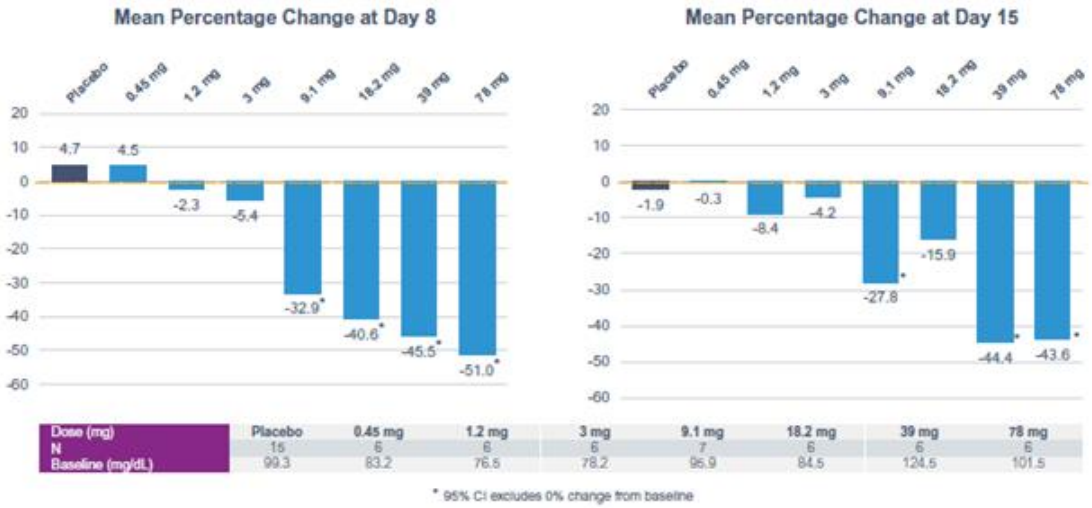


Figure 25: Changes in Triglycerides after Single Dose of BIO89-100

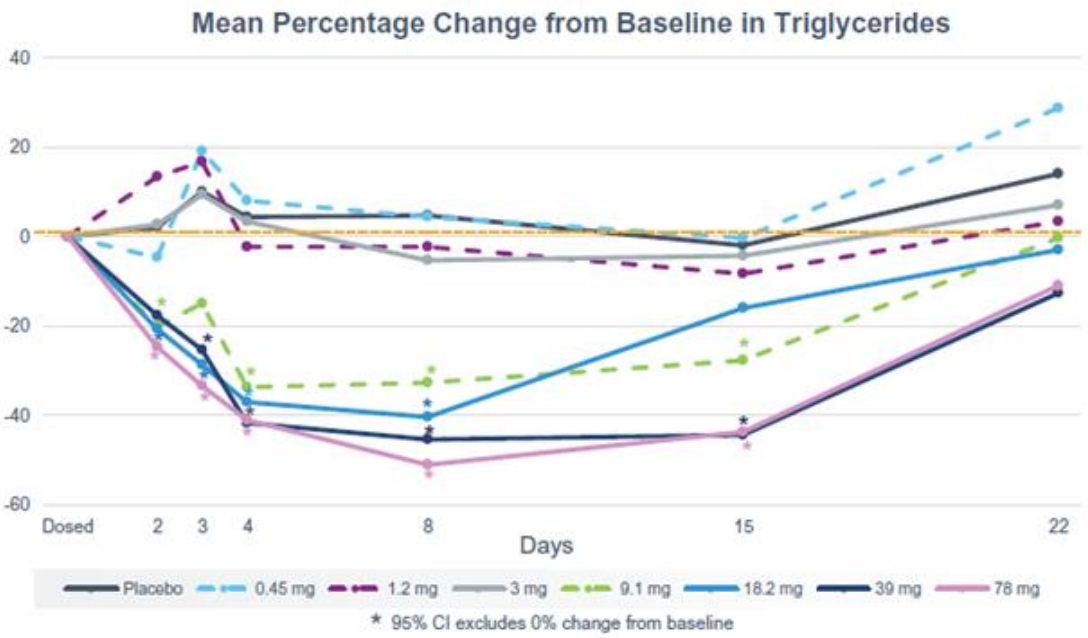
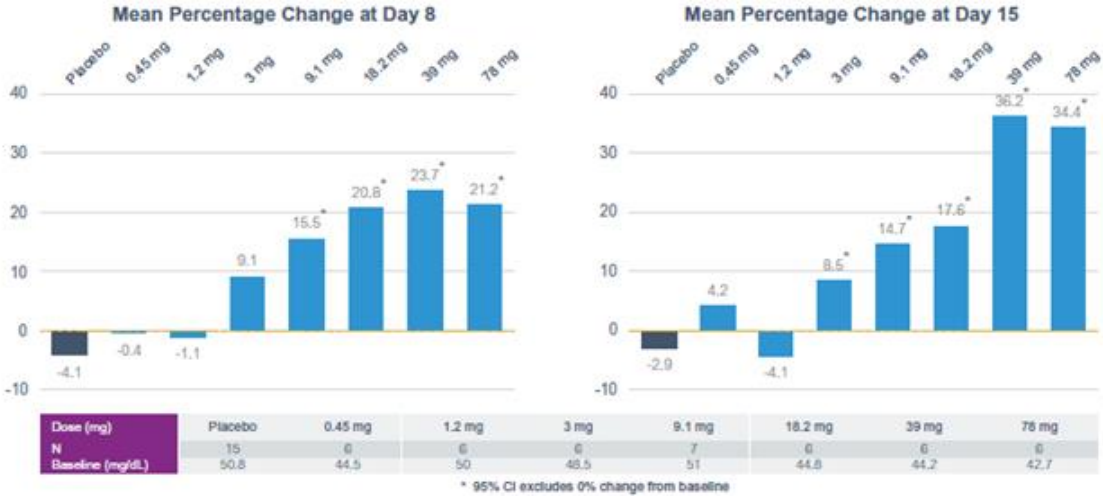


Figure 26: Changes in LDL Cholesterol after Single Dose of BIO89-100

Figure 27: Changes in HDL Cholesterol after Single Dose of BIO89-100



BIO89-100 was well tolerated across the dose range in our Phase 1a clinical trial. There were no deaths, serious adverse events or discontinuations due to adverse events. The most commonly observed treatment-related adverse events, occurring in at least two subjects in the pooled BIO89-100 group, were injection site reactions and headache, all of which were reported as mild. Injection site reactions were more frequent in the 39 mg cohort, likely due to a larger injection volume administered at one time in that cohort. No clinically meaningful trends were observed in gastrointestinal events, laboratories or vital signs including blood pressure or heart rate changes. No tremors were reported. Five of 43 BIO89-100 treated subjects tested positive for anti-drug antibodies ("ADA"); however, all titers were low (≤ 16) and did not appear to affect the PK or safety profile.

Treatment-related treatment emergent adverse events ("TEAE") reported in two subjects or more in pooled BIO89-100 treatment group are shown in Figure 28 below.

Figure 28: Treatment-Related TEAE Reported in ≥ 2 Subjects in Pooled BIO89-100 Treatment Group

	Placebo	BIO89-100							Pooled
	(N=15)	0.45 mg	1.2 mg	3 mg	9.1 mg	18.2 mg	39 mg	78 mg	BIO89-100
n (%)		(N=6)	(N=6)	(N=6)	(N=7)	(N=6)	(N=6)	(N=6)	(N=43)
Any Treatment Related TEAE	3 (20.0)	0	0	0	1	3	6	3	13 (30.2)
Injection site induration	1 (6.7)	0	0	0	1	0	5	1	7 (16.3)
Injection site erythema	1 (6.7)	0	0	0	0	0	3	2	5 (11.6)
Injection site pain	0	0	0	0	0	0	2	0	2 (4.7)
Headache	1 (6.7)	0	0	0	0	2	0	0	2 (4.7)

These data supported the advancement of BIO89-100 into a study in patients with NASH or patients with NAFLD and a high risk of NASH to evaluate BIO89-100's potential as a treatment of NASH. Based on PK/ PD modeling and drug exposure analysis, we have identified BIO89-100 doses in the range of 9 mg to 36 mg weekly ("QW") or every other week ("Q2W") as the target dose range for evaluation in future clinical trials in patients with NASH or patients with NAFLD and a high risk of NASH.

We believe that the totality of the data from our Phase 1a study, the preclinical data with BIO89-100 and the clinical data from third parties collectively support the hypothesis that BIO89-100 has the potential to address the complex nature of NASH, especially given the frequency of metabolic co-morbidities in NASH patients. The magnitude and significance of BIO89-100's biological effects after a single dose on lipid parameters in healthy volunteers were observed to be robust and durable, and the magnitude of these reductions appear to be comparable or better than data reported to date in Phase 1 clinical trials of other FGF analogs, although no head-to-head studies have been conducted.

Phase 1b/2a POC Clinical Trial

In the second quarter of 2020, we expect to complete patient enrollment in our Phase 1b/2a POC clinical trial. Our clinical trial is a multicenter, randomized, double-blind, placebo-controlled, multiple ascending dose-ranging trial in patients with NASH or patients with NAFLD and a high risk of NASH, with 83 total patients randomized to receive QW or Q2W subcutaneous dosing of BIO89-100 or placebo for up to 12 weeks. This clinical trial is designed to assess the safety, tolerability and PK properties of BIO89-100 as well as change in liver fat measured by MRI-PDFF and key biomarker assessments. These data are aimed at providing proof-of-concept for BIO89-100 in NASH and help inform dose selection for larger, longer-term paired-biopsy trials. At our meeting with the FDA in June 2019, the FDA concurred with our overall trial design, including study population, dose selection and study treatment duration.

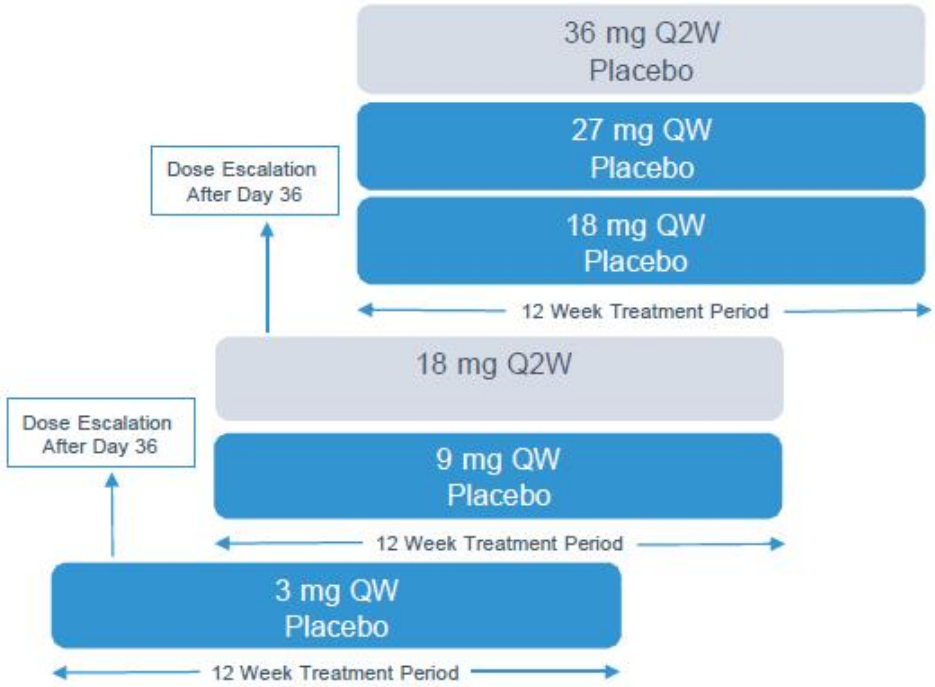
Our POC study is enrolling patients with NASH or patients with NAFLD and a high risk of NASH, defined as patients with steatosis greater than 10% who have central obesity and Type 2 diabetes or central obesity and evidence of liver injury. NAFLD patients, especially the subset of NAFLD patients we will enroll, have similar disease characteristics as patients with biopsy-proven NASH, and we expect that the data from these NAFLD patients will be informative regarding the potential of BIO89-100 as treatment for NASH. The trial will include a set number of patients with biopsy confirmed NASH with fibrosis (F1-F3) to help inform the design of subsequent clinical trials.

The key objectives of the trial are to:

- evaluate the safety and tolerability of multiple ascending doses of BIO89-100;
- assess change from baseline in liver fat (measured via MRI-PDFF);
- assess changes from baseline in lipids, glycemic control parameters, fibrosis and inflammation markers;
- characterize the PK properties of BIO89-100; and
- evaluate the immunogenicity of BIO89-100 as measured by presence of ADA.

The design of the trial is presented in Figure 29 below:

Figure 29: POC Clinical Trial Design



Our planned active treatment groups are: 3 mg, 9 mg 18 mg and 27 mg QW, and 18 mg and 36 mg Q2W. In February 2020 we completed the second dose escalation and began enrolling patients in the final three dose cohorts. We have designed the trial to detect differences on MRI-PDFF between BIO89-100 at different dose levels and the pooled placebo group. We expect to report topline data in the second half of 2020. In addition, we anticipate initiating a Phase 2b trial in the first half of 2021.

BIO89-100 Differentiation

We believe BIO89-100 could have a differentiated profile relative to other therapies targeting FGF21 and FGFR1c that are in development.

A PEGylated form of FGF21 is currently in two third-party Phase 2b studies in NASH. The compound has a reported half-life of 19 to 24 hours and includes mutations with non-native amino acid substitutions. In this third party's Phase 2a study, the molecule showed a significant reduction in absolute liver fat measured by MRI-PDFF and a significant decrease in concentration of PRO-C3 (a biomarker of fibrosis), but no significant changes on lipid markers. Study outcomes were better when dosed as a daily injection versus a weekly injection. The compound was deemed generally well tolerated, although a higher frequency of gastrointestinal adverse events was reported in treated patients. Sixty-three percent to 92% of treated patients in the Phase 2a study tested positive for anti-drug and anti-FGF21 antibodies.

A second compound, a long-acting Fc-FGF21 fusion protein with extended half-life of approximately three to four days, has completed third-party Phase 1 studies in which patients with Type 2 diabetes demonstrated decreases in triglycerides and increases in HDL-C, with improvements in insulin sensitivity, but modest to no changes in LDL in doses approximating those advancing to further development. The highest doses tested in the single and multiple-ascending dose study were not well-tolerated with adverse events of significance being gastrointestinal disorders and tremors. The compound is currently in a Phase 2a study in NASH with weekly dosing.

A third compound, an agonistic antibody selectively activating FGFR1c and its co-receptor ß-Klotho, has completed a third-party Phase 1 study as a once-monthly injectable insulin sensitizer for the treatment of NASH. Reductions in liver fat content and improvements in metabolic parameters were reported in a clinical trial evaluating a high single dose in obese, insulin-resistant, non-diabetic subjects with NAFLD. The most common adverse events reported were injection site reaction and increased appetite. Subjects gained an average of 1.6 kg body weight 36 days after dosing compared to baseline. The compound agonizes only the FGFR1c receptor and is not believed to have any activity on the FGFR2c and FGFR3c receptors.

We believe BIO89-100 may be a differentiated FGF21 therapy based on its robust and durable biological effects and a favorable tolerability profile. In addition, BIO89-100 has the potential for a once every two-weeks dosing interval that could provide significant value to asymptomatic patients who will be taking the product chronically. In market research that we conducted amongst obese diabetic subjects (n=150), respondents were asked for their preference when selecting an injectable product with different dosing regimens for the treatment of a chronic liver condition. In this study, 63% of respondents expressed a preference or strong preference for a product injected once every two weeks versus a product injected every week, and 68% of respondents expressed similar preferences for a product injected once every two weeks versus a product injected daily. Further, we believe that BIO89-100 may have a differentiated tolerability profile and that tolerability issues may influence physician and patient preference in NASH, a chronic and generally asymptomatic disease. We believe the risk of CNS effects, significant gastrointestinal tolerability issues and weight gain could significantly impact adoption by physicians and patients. Finally, based on the non-human primate study results and the human SAD study results across different lipid markers (triglyceride reduction up to 51% and LDL reduction up to 37%), we believe BIO89-100 may offer robust and durable biological effects. We believe that activation of the FGFR1c, 2c and 3c receptors may confer benefits versus activation of a single receptor (FGFR1c) given the expression of the receptors in the key organs of interest (FGFR1c in adipose tissue and FGFR2c and FGFR3c in the liver) and provide a more balanced approach.

Severe Hypertriglyceridemia

We also intend to develop BIO89-100 for the treatment of SHTG. Hypertriglyceridemia (“HTG”) is characterized by elevated fasting plasma triglyceride levels higher than 200 mg/dL and SHTG is typically defined as triglyceride levels of greater than or equal to 500 mg/dL. SHTG is associated with an increased risk of NAFLD, NASH and cardiovascular diseases, as well as acute pancreatitis, accounting for up to 10% of all acute pancreatitis episodes. A recent third-party study utilizing an omega-3 fatty acid (“omega-3 FA”) demonstrated the linkage between a reduction in triglycerides and favorable cardiovascular clinical outcomes.

It is estimated that there are 2.5 million to 4 million patients in the United States with triglyceride levels of greater than or equal to 500 mg/dL. Of these patients, it is estimated that 42% have dyslipidemia and 27% have diabetes. This patient population is expected to increase due to the triple epidemic of obesity, metabolic syndrome and Type 2 diabetes. In addition, the addressable market has the potential to expand as a result of increasing awareness of the importance of treating elevated TG levels, similar to the focus today of physicians on managing LDL levels, as well as due to third party commercial efforts expected to promote TG reduction.

The treatment regimen for SHTG includes dietary restrictions and lipid-lowering drug treatment such as fibrates, omega-3 fish oils and niacin. Some statins are indicated in HTG but do not have an indication for use in SHTG. In third-party studies, up to 50% of treated SHTG patients were unable to reduce their triglyceride levels to < 500 mg/dL despite using approved drugs and are considered refractory patients. These refractory patients have substantial unmet medical need and represent a significant market opportunity as there are no approved therapies for the treatment of refractory SHTG.

Despite multiple agents approved for the treatment of SHTG, these agents have limitations that may not make them ideal for all patients. For example, fibrates have demonstrated reductions in triglycerides of up to approximately 55% at 12 weeks of treatment. However, they have also shown increases in LDL-C (up to 45%), a detrimental effect in this patient population, risk of drug-drug interactions and increases in transaminases, as well as tolerability issues including myopathy. Omega 3 fish oils have shown more modest benefits in reduction of triglycerides from baseline of approximately 25% to 45%. However, fish oils with a higher percentage reduction in triglycerides have also showed major increases in LDL-C (up to 45%). Fish oils also have a significant pill burden given the high daily doses required. In addition, these agents fail to meaningfully address the related co-morbidities of SHTG, including glycemic control, which, when left untreated, may further exacerbate the condition. Yet, despite these limitations, the existing drugs have achieved commercial success with two third parties each generating peak sales of approximately $1 billion or greater. While we believe BIO89-100 has the potential to address the co-morbidities of SHTG, there is no guarantee that it would earn comparable peak sales if it is approved by the FDA. Given the continuing unmet need in SHTG and limitations of current treatments, there are several agents in development for the treatment of SHTG, including a fish oil product, a fibrate, and novel drugs primarily targeting rare, genetically defined subsets of SHTG, including ANGPTL3 and ApoC III inhibitors. Dyslipidemia apart from SHTG also continues to be a very active area for pharmaceutical development. We believe BIO89-100 may be a differentiated SHTG therapy due to its pleiotropic metabolic benefits and its potential to target a broader patient population versus those therapies primarily targeting rare, genetically defined subsets of SHTG.

BIO89-100 has demonstrated significant reduction in triglyceride levels in both its non-human primate studies and our Phase 1a clinical study. In diabetic obese cynomolgus monkeys with elevated triglyceride levels, BIO89-100 showed significant effects on triglycerides with a maximal reduction of 78% and 76% at doses of 1 mg/kg (see Figures 15 and 21). In monkeys treated with baseline levels of triglycerides > 500mg/dL (n=4), the three monkeys treated with BIO89-100 1 mg/kg weekly had TG reductions > 90% at study end. In our Phase 1a clinical study, in patients with baseline triglyceride values in the normal range (mean baseline 94 mg/dL), BIO89-100 demonstrated reductions of triglycerides from baseline up to 51% at Day 8 after a single dose in healthy volunteers. While currently approved SHTG therapies decrease TG levels, they generally do not have broader metabolic benefits. In our Phase 1a study, BIO89-100 demonstrated a reduction in LDL of up to 37% (see Figure 26) and to the extent that we are able to show in subsequent human clinical trials that BIO89-100 significantly decreases both TG and LDL-C levels and improves other metabolic parameters, such as glycemic control, we believe that BIO89-100 could be a differentiated therapy in this indication. Based on a mechanism of action that is distinct from the currently approved therapies, we believe that BIO89-100 has the potential to be used as a monotherapy agent or in combination with other agents. Another FGF21 analog developed by a third party has also demonstrated a statistically significant reduction in triglycerides in obese, Type 2 diabetes patients. We intend to initiate a Phase 2 trial in SHTG patients in the first half of 2020 in order to evaluate the ability of BIO89-100 to reduce triglyceride levels compared to baseline levels and to report topline data in the first half of 2021. Secondary endpoints will evaluate other lipids, high sensitivity C-reactive Protein (hsCRP), glucose, body weight, safety, and pharmacokinetics. We expect this Phase 2 trial to enroll approximately 90 patients with triglyceride levels greater than or equal to 500 mg/dL at baseline and include both patients on no background triglyceride lowering therapy or on a stable dose of statin and/or prescription fish oil. Patients will be randomized to receive multiple doses of BIO89-100 or placebo for six to eight weeks.

There is regulatory precedence in the United States for the approval of therapies to treat SHTG based on such therapies demonstrating a reduction in triglycerides from baseline at 12 weeks. The FDA surrogate endpoint table for drug approval lists a reduction in triglycerides from baseline as the endpoint for full approval of a therapy in SHTG. A clinical outcome study was not required for certain third-party approvals in SHTG or as a post-marketing commitment. The SHTG Phase 3 trial for some of these products consisted of a single study of a 12-week duration with 75 to 100 patients per treatment group. Based on current plans, we anticipate initiating a registrational trial in SHTG patients by the end of 2021, which we expect will follow existing SHTG regulatory precedence.

Based on FDA guidance for the development of SHTG treatments, as well as the regulatory path followed by other companies that have successfully developed SHTG therapies, we believe that a combination of smaller clinical trials and shorter development timelines could mean that SHTG potentially represents a quicker path to market for BIO89-100.

Agreements with Teva

Agreements Relating to FGF21 Program

On April 16, 2018, we entered into an Asset Transfer and License Agreement (the "FGF21 Agreement") with Teva Pharmaceutical Industries Ltd ("Teva"), under which we acquired certain patents, intellectual property and other assets relating to Teva's glycoPEGylated FGF21 program. Under this agreement, Teva also granted a perpetual, non-exclusive (but exclusive as to BIO89-100), non-transferable, worldwide license to patents and know-how related to glycoPEGylation technology for use in the research, development, manufacture and commercialization of the compound BIO89-100 and products containing BIO89-100. In addition, we entered into a Sublicense Agreement with ratiopharm (the "ratiopharm Sublicense"), under which we were granted a perpetual, exclusive, worldwide sublicense to patents and know-how related to glycoPEGylation technology used in the development, manufacture and commercialization of BIO89-100 and products containing BIO89-100.

Under the FGF21 Agreement, we are obligated to use commercially reasonable efforts to develop and commercialize BIO89-100 in each of the United States and five major European countries. We have the right to sublicense all rights licensed to us by Teva under the FGF21 Agreement.

Pursuant to the FGF21 Agreement and the FASN Agreement (as defined and described below), we paid Teva a nonrefundable upfront payment of $6.0 million. In addition, under the FGF21 Agreement, we are required to make certain payments to Teva totaling $2.5 million for the achievement of certain clinical development milestones, and additional payments totaling up to $65.0 million upon achievement of certain commercial milestones. We are also obligated to pay Teva tiered royalties at percentages in the low-to-mid single-digits on worldwide net sales of products containing BIO89-100. Our royalty obligations will terminate, on a product-by-product and country-by-country basis, at the later of: (1) the date of expiration of the last to expire valid claim in the assigned patents that covers BIO89-100 in such country, (2) the expiration of data or regulatory exclusivity for BIO89-100 in such country and (3) 10 years from the first commercial sale of BIO89-100 in such country. We are not required to make any payments to ratiopharm pursuant to the ratiopharm Sublicense.

The term of the FGF21 Agreement will continue, on a product-by-product and country-by-country basis, until the royalty term with respect to BIO89-100 in such country expires. The ratiopharm Sublicense will continue until terminated in accordance with its terms. We may terminate the FGF21 Agreement and the ratiopharm Sublicense for any reason. Either party may terminate the FGF21 Agreement for cause for the other party's uncured material breach. ratiopharm may terminate the ratiopharm Sublicense for certain material breaches by us. Either party may terminate the FGF21 Agreement or the ratiopharm Sublicense in the event of bankruptcy of the other party. Teva may terminate the FGF21 Agreement if we challenge the validity of any patent licensed to us under the FGF21 Agreement. Termination of the FGF21 Agreement or the ratiopharm Sublicense will impact our rights under the intellectual property licensed to us by Teva and ratiopharm, respectively, but will not affect our rights under the assets assigned to us.

On April 16, 2018, we also entered into a Reagent Supply and Technology Transfer Agreement, under which Teva will supply us with certain reagents required for the glycoPEGylation process that are necessary for our development and commercialization of BIO89-100, and transfer to us certain know-how required for the production of such reagents. The term of this agreement was recently extended by mutual agreement until December 31, 2022.

FASN Agreements

On April 16, 2018, we entered into an Asset Transfer and License Agreement with Teva under which we acquired from Teva patents, intellectual property and other assets relating to Teva's development program of small molecule inhibitors of FASN (the "FASN Agreement"). Under the FASN Agreement we are obligated to use commercially reasonable efforts to develop and commercialize FASN in the United States and five major European countries. We have the right to sublicense all rights licensed to us by Teva under the FASN Agreement.

Pursuant to the FASN Agreement and the FGF21 Agreement (as described above), we paid Teva a nonrefundable upfront payment of $6.0 million. In addition, under the FASN Agreement, we are required to make certain payments to Teva totaling $2.5 million for the achievement of certain clinical development milestones, and additional payments totaling up to $65.0 million upon achievement of certain commercial milestones. We are also obligated to pay Teva tiered royalties at percentages in the low-to-mid single-digits on worldwide net sales of products arising from the FASN program. Our royalty obligations will terminate, on a product-by-product and country-by-country basis, at the later of: (1) the date of expiration of the last to expire valid claim in the assigned patents that covers FASN in such country, (2) the expiration of data or regulatory exclusivity for such product arising from the FASN program in such country and (3) 10 years from the first commercial sale of a product arising from the FASN program in such country.

The term of the FASN Agreement will continue, on a product-by-product and country-by-country basis, until the royalty term with respect to the product arising from the FASN program in such country expires. We may terminate the FASN Agreement for any reason. Either party may terminate the agreement for cause for the other party's uncured material breach, or in the event of bankruptcy of the other party.

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 investigational new drug ("IND") application, 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 biologics license application ("BLA") after completion of all pivotal clinical trials;
- satisfactory completion of an FDA Advisory Committee review, if applicable;
- 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 pre-approval inspection of the manufacturing facility or facilities at which the proposed product is produced to assess compliance with 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, we must submit an IND to the FDA. An IND is a request for authorization from the FDA to administer an investigational new drug product to humans. The central focus of an IND submission is 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, PK, pharmacology and PD 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 so called Phase 4 studies 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, must develop methods for testing the identity, strength, quality and purity of the final product, or for biologics, the safety, purity and potency. 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'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 postmarket 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.

Expedited Programs for Serious Conditions

The FDA maintains several programs intended to facilitate and expedite development and review of new drugs and biologics to address unmet medical needs in the treatment of serious or life-threatening diseases or conditions. These programs include Fast Track designation, Breakthrough Therapy designation, Priority Review and Accelerated Approval. These programs can significantly reduce the time it takes for the FDA to review a BLA, but they do not guarantee that a product will receive FDA approval. Even if a product qualifies initially, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review will not be shortened. In May 2018, the Right to Try Act also established a program to increase access to unapproved, investigational treatments for patients diagnosed with life-threatening diseases or conditions who have exhausted approved treatment options and who are unable to participate in a clinical trial.

A new drug or biologic is eligible for Fast Track designation if it is intended to treat a serious or life- threatening disease or condition and demonstrates the potential to address unmet medical needs for such disease or condition. Fast Track designation provides increased opportunities for sponsor interactions with the FDA during preclinical and clinical development, in addition to the potential for rolling review once a marketing application is filed, meaning that the agency may review portions of the marketing application before the sponsor submits the complete application, as well as Priority Review, discussed below. In addition, a new drug or biologic may be eligible for Breakthrough Therapy designation if it is intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Breakthrough Therapy designation provides all the features of Fast Track designation in addition to intensive guidance on an efficient drug development program beginning as early as Phase 1, and FDA organizational commitment to expedited development, including involvement of senior managers and experienced review staff in a cross-disciplinary review, where appropriate.

Any product submitted to the FDA for approval, including a product with Fast Track or Breakthrough Therapy designation, may also be eligible for additional FDA programs intended to expedite the review and approval process, including Priority Review designation and accelerated approval. A product is eligible for Priority Review if it has the potential to provide a significant improvement in safety or effectiveness in the treatment, diagnosis or prevention of a serious disease or condition. Under priority review, FDA will review an application in six months compared to ten months for a standard review. Products are eligible for accelerated approval if they can be shown to have an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or an effect on a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality which 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 treatment. Accelerated approval is usually contingent on a sponsor's agreement to conduct additional post-approval studies to verify and describe the product's clinical benefit. In addition, unless otherwise informed by the FDA, the FDA currently requires, as a condition for accelerated approval, that all advertising and promotional materials that are intended for dissemination or publication be submitted to FDA for review before the initial dissemination or publication.

Post-Approval Requirements

Any products manufactured or distributed by us 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 us and our 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 us and any 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 by us 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 of 2010 (collectively, the "Affordable Care Act"), 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. To date, a number of biosimilars have been licensed under the BPCIA, and numerous biosimilars have been approved in Europe. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars.

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. Complexities associated with the larger, and often more complex, structures of biological products, as well as the processes by which such products are manufactured, pose significant hurdles to implementation of the abbreviated approval pathway that are still being worked out by the FDA.

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. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

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, implementation, and impact 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 & Medicaid Services ("CMS"), other divisions of the U.S. 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 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 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. The statutory exceptions and regulatory safe harbors are also subject to change.

Additionally, the intent standard under the Anti-Kickback Statute was amended by the Affordable Care Act, 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 Affordable Care Act also 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 FCA (discussed below).

The federal false claims laws, including the FCA, which imposes significant penalties and can be enforced by private citizens through civil qui tam actions, and civil monetary penalty laws 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. Although we would not submit claims directly to payors, manufacturers can be held liable under these laws if they are deemed to "cause" the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customers or promoting a product off-label. In addition, our future activities relating to the reporting of wholesaler or estimated retail prices for our products, the reporting of prices used to calculate Medicaid rebate information and other information affecting federal, state, and third-party reimbursement for our products, and the sale and marketing of our products, are subject to scrutiny under this law. For example, pharmaceutical companies have been prosecuted under the FCA in connection with their alleged off-label promotion of drugs, purportedly concealing price concessions in the pricing information submitted to the government for government price reporting purposes, and allegedly providing free product to customers with the expectation that the customers would bill federal health care programs for the product.

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 Affordable Care Act 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.

In addition, we may be subject to data privacy, data security and data breach notification laws, regulations, standards, and codes of conduct by both the U.S. federal government and the states. These laws, regulations, standards, and codes of conduct may govern the collection, use, disclosure and protection of health-related and other personal information. HIPAA, as amended by the HITECH, imposes requirements relating to the privacy, security and transmission of individually identifiable health information. HIPAA requires covered entities to limit the use and disclosure of protected health information to specifically authorized situations, and requires covered entities to implement security measures to protect health information that they maintain in electronic form. The federal government may impose civil, criminal, and administrative fines and penalties and/ or additional reporting or oversight obligations for a violation of HIPAA's requirements. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to business associates 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 to HIPAA and HITECH, 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 federal law, and may have a more prohibitive effect than federal law, 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 the part of Medicare that 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.

Additionally, the federal Physician Payments Sunshine Act (the "Sunshine Act") within the Affordable Care Act, 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, as defined by such law, 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. This information is made publicly available on a CMS website, and failure to report accurately could result in penalties. In addition, many states also govern the reporting of 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 state and local laws have been enacted 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. In addition, 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 significant penalties, including without limitation, civil, criminal and/or administrative penalties, damages, fines, disgorgement, 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, private 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 European Union, 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 has 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 Affordable Care Act has substantially changed healthcare financing and delivery by both governmental and private insurers. The Affordable Care Act and its implementing regulations, among other things, revised the methodology for calculating rebates for covered outpatient drugs and certain biologics owed by manufacturers to the state and federal government under the Medicaid Drug Rebate Program, increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program, extended the Medicaid Drug Rebate program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations, subjected manufacturers to new annual fees and taxes for certain branded prescription drugs, and expanded programs designed to test innovative payment models, service delivery models, or value-based arrangements, and fund comparative effectiveness research.

There remain legal and political challenges to certain aspects of the Affordable Care Act. Since January 2017, President Trump has signed executive orders and other directives designed to delay, circumvent or loosen certain requirements mandated by the Affordable Care Act. On December 22, 2017, President Trump signed into law the Tax Cuts and Jobs Act of 2017 (the “Tax Act”), which included a provision that repealed the tax penalty for an individual’s failure to maintain Affordable Care Act-mandated health insurance, effective January 1, 2019.

Further, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the Affordable Care Act’s mandated “Cadillac” tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminates the health insurer tax.

Moreover, the Bipartisan Budget Act of 2018 (the “BBA”) among other things, amended the Affordable Care Act, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the “donut hole.” Additionally, in December 2018, CMS published a final rule permitting further collections and payments to and from certain Affordable Care Act qualified health plans and health insurance issuers under the Affordable Care Act risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment.

On December 14, 2018, a United States District Court judge in Texas ruled that the Affordable Care Act is unconstitutional in its entirety because the “individual mandate” was repealed by Congress as part of the Tax Cuts and Jobs Act of 2017. The decision was been appealed to the United States Court of Appeals for the Fifth Circuit and on December 18, 2019, the United States Court of Appeals for the Fifth Circuit upheld the District Court’s ruling that the individual mandate was unconstitutional, but remanded the case back to the District Court to determine whether the remaining provisions of the Affordable Care Act were nonetheless valid. On March 2, 2020, the United States Supreme Court granted the petitions for writs of certiorari to review this case, and has allotted one hour for oral arguments, which are expected to occur in the fall. It is unclear how such litigation and other efforts to repeal and replace the Affordable Care Act will impact the Affordable Care Act.

We anticipate that the Affordable Care Act, 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.

In addition, 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 Affordable Care Act was enacted. For example, in August 2011, President Obama signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals in spending reductions. The Joint Select Committee on Deficit Reduction did not achieve a targeted deficit reduction of at least $1.2 trillion for fiscal years 2012 through 2021, triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect beginning on April 1, 2013 and which, under the Bipartisan Budget Act of 2019, have been extended through 2029, subject to additional Congressional action. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

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. At the federal level, the Trump administration's budget proposal for fiscal year 2021 includes a $135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. On March 10, 2020, the Trump administration sent "principles" for drug pricing to Congress, calling for legislation that would, among other things, cap Medicare Part D beneficiary out-of-pocket pharmacy expenses, provide an option to cap Medicare Part D beneficiary monthly out-of-pocket expenses, and place limits on pharmaceutical price increases. Previously, the Trump administration released a "Blueprint," or plan, to lower drug prices and reduce out of pocket costs of drugs that contained 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.

HHS has solicited feedback on some of these measures and has implemented others under its existing authority. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage plans the option to use step therapy for Part B drugs beginning January 1, 2020. This final rule codified CMS's policy change that was effective January 1, 2019. Further, in December 2019, the FDA issued draft guidance describing procedures for drug manufacturers to facilitate the importation of FDA-approved drugs and biologics manufactured abroad and originally intended for sale in a foreign country into the United States. President Trump's administration has also proposed to establish an international pricing index that would tie domestic prices for certain drugs and biologics to the prices in other countries. While some proposed measures may require additional 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. For example, after some pharmacy benefit managers and insurers adopted policies stating that the amount of a copay coupon would not be applied to the enrollee's deductible or out-of-pocket maximum (referred to as "accumulator adjustment programs"), some states passed legislation banning these policies. On January 31, 2020, CMS released its proposed 2021 Notice of Benefit and Payment Parameters rule, which provides that insurers would no longer be required to count any coupons from drug manufacturers towards a consumer's out-of-pocket limit. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our product candidates, if approved.

Additional Regulation

In addition to the foregoing, local, state and federal laws, including in the United States and Israel, regarding such matters as safe working conditions, manufacturing practices, environmental protection, fire hazard control 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. If our operations result in contamination of the environment or expose individuals to hazardous or biohazardous substances, we could be liable for damages, environmental remediation, and/or governmental fines. We believe that we are in material compliance with applicable environmental laws and occupational health and safety laws 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. We may incur significant costs to comply with such laws and regulations now or in the future.

Competition

The biopharmaceutical industry is intensely competitive and subject to rapid innovation and significant technological advancements. We believe the key competitive factors that will affect the development and commercial success of BIO89-100 and any future product candidates are efficacy, safety and tolerability profile, reliability, convenience of dosing, price, the level of generic competition and reimbursement. Our competitors include multinational pharmaceutical companies, specialized biotechnology companies, universities and other research institutions. A number of biotechnology and pharmaceutical companies are pursuing the development or marketing of pharmaceuticals that target the same diseases that we are targeting. Smaller or earlier-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. Given the high incidence of NASH, it is likely that the number of companies seeking to develop products and therapies for the treatment of liver and cardio-metabolic diseases, such as NASH, will increase.

If BIO89-100 is 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 plc; GS-0976, an ACC inhibitor, and GS-9674, an FXR agonist, from Gilead Sciences, Inc.; PF-05221304, an ACC inhibitor, and PF-06835919, a KHK inhibitor, from Pfizer Inc.; Ocaliva, an FXR agonist from Intercept Pharmaceuticals, Inc.; resmetirom, a beta-thyroid hormone receptor agonist from Madrigal Pharmaceuticals, Inc.; VK2809, a beta-thyroid hormone receptor agonist from Viking Therapeutics, Inc.; aldfermin, an FGF19 analog from NGM Biopharmaceuticals, Inc.; MK-3655, an FGFR1c/KLB agonist antibody from Merck & Co., Inc.; pegbelfermin, a PEGylated FGF21 analog from Bristol-Myers Squibb Company; AKR-001, a FGF21 fusion protein from Akero Therapeutics, Inc.; elobixibat, an IBAT-inhibitor from Albireo Pharma, Inc.; a Galectin-3 inhibitor from Galectin Therapeutics Inc.; a synthetic conjugate of cholic acid and arachidic acid from Galmed Pharmaceuticals Ltd.; an FXR agonist from Metacrine, Inc.; FXR agonists from Novartis AG; a mitochondrial pyruvate complex modulator from Cirius Therapeutics, Inc.; semaglutide, a GLP-1 receptor agonist from Novo Nordisk A/S; tirzepatide, a dual IP/GLP-1 receptor agonist from Eli Lilly and Company; and elafibranor, a PPAR alpha/delta agonist from Genfit S.A.

If BIO89-100 is approved for the treatment of SHTG, we would face competition from currently approved and marketed products, including statins, fibrates, Vascepa, Epanova and Lovaza, as well as generic products. Further competition could arise from products currently in development, including: AKCEA-APOCIII-LRx, an ApoC III inhibitor and AKCEA-ANGPTL3, an anti-ANGPTL3 from Akcea Therapeutics, Inc.; evinacumab, an Anti-ANGPTL3 from Regeneron Pharmaceuticals, Inc.; pemafibrate, a PPAR alpha agonist from Kowa Research Institute, Inc.; gemcabene; CaPre, an omega-3 fatty acid from Acasti Pharma Inc.; and ARO-APOC3, an ApoC III inhibitor and ARO-ANG3, an anti-ANGPTL3 from Arrowhead Pharmaceuticals, Inc.

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 longer operating histories and greater experience than we have in undertaking nonclinical studies and human clinical trials of new pharmaceutical products and in obtaining regulatory approvals of human therapeutic products. Many of our competitors have established distribution channels for 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. As a result, our competitors may obtain regulatory approval of their products more rapidly than we do or may obtain patent protection or other intellectual property rights that limit our ability to develop or commercialize our product candidate or any future product candidates. Our competitors may also develop and succeed in obtaining approval for 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 we are 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 candidate or any future 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 enrolling patients for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Manufacturing and Supply

We do not own or operate manufacturing facilities for the production of BIO89-100, nor do we have plans to develop our own manufacturing operations in the foreseeable future. We currently rely, and expect to continue to rely, on third parties for the manufacturing of our product candidates for preclinical and clinical testing, as well as for commercial manufacturing if BIO89-100 or any future product candidate receives marketing approval.

BIO89-100 drug substance is manufactured by fermentation of a recombinant strain of the bacterium E. coli. Product accumulates as insoluble particles (inclusion bodies) within the cells and is recovered by cell disruption, followed by solubilization of the inclusion bodies, protein refolding and purification with two chromatographic separation columns. Purified material is glycoPEGylated in a 2-step enzymatic reaction where a 20kDa linear glycoPEG moiety is attached to the protein through GalNAc and Sialic Acid linkers.

GlycoPEGylated protein is purified with two chromatographic columns to yield product with target quality attributes. Purified glycoPEGylated protein is concentrated and then formulated to a target concentration with formulation buffer as drug product.

BTPH is our sole source supplier for BIO89-100. While any reduction or halt in supply of drug product from BTPH could limit our ability to develop BIO89-100 until a replacement contract manufacturer is found and qualified, we have recently produced several batches to support toxicology and clinical studies. We currently have material available to support our ongoing Phase POC 1b/2a trial of BIO89-100 for the treatment of NASH and for our SHTG trial.

We are working with BTPH on process optimization to support large-scale production for future trials and commercialization. In parallel, we have entered into a contract with a formulation development company to explore the potential for a new refrigerated liquid formulation and/or a freeze-dried, or lyophilized product.

BTPH Agreement

On May 7, 2018, we entered into a master services agreement with BTPH, under which BTPH agreed to provide us certain services, including the manufacturing, packaging, labeling and storing of BIO89-100, under statements of work for such services to be agreed by the parties from time to time. The master services agreement will continue for the duration of time that BTPH is providing services to us, unless earlier terminated by either party upon its terms. We may terminate the agreement at any time after a specified notice period and subject to the payment of certain agreed upon fees where such termination results in cancellation of manufacturing scheduled within a certain period. In addition, either party may terminate the agreement for cause for the other party's uncured material breach, in the event of bankruptcy of the other party, in the event of the commission of fraud by the other party or in the event of a force majeure.

Sales and Marketing

We currently have no marketing, sales or distribution capabilities. In order to commercialize any products 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 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.

We plan to seek third-party support from established pharmaceutical and biotechnology companies 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 upon our ability to protect our core technology and intellectual property. To protect our intellectual property rights, we rely on patents, trademarks, copyrights and trade secret laws, confidentiality procedures, and employee disclosure and invention assignment agreements. Our intellectual property is critical to our business and we strive to protect it through a variety of approaches, including by obtaining and maintaining patent protection in the United States and internationally for our product candidates, novel biological discoveries, new targets and applications, and other inventions that are important to our business. For our product candidates, we generally intend to pursue patent protection covering compositions of matter, methods of making and methods of use. As we continue the development of our product candidates, we plan to identify additional means of obtaining patent protection that would potentially enhance commercial success, including pursuit of claims directed to new therapeutic indications.

FGF21 Patents

Our FGF21 patent portfolio includes two families: the first is entitled "Remodeling and GlycoPEGylation of Fibroblast Growth Factor (FGF)" and the second is entitled "Mutant FGF-21 Peptide Conjugate and Uses Thereof." The first family provides granted patent protection in 39 countries around the globe, including the United States (U.S. Patent Number 9,200,049; expiry June 25, 2028), Canada, Europe (broadly), and Japan (latter three expire October 31, 2025) for FGF21 conjugates comprising a variety of modifying groups that can be attached at several different amino acid positions. GlycoPEGylated FGF21 is specifically claimed. The granted claims broadly protect our lead drug candidate BIO89-100 and pharmaceutical compositions thereof, as well as methods for making and using BIO89-100 to treat FGF21 deficiency in a patient in need thereof. One U.S. application is pending in this family.

The second family is specifically directed to BIO89-100. The progenitor PCT Application for this family was filed on September 4, 2018 (PCT/IB2018/00112). A U.S. Prioritized Examination Continuation Patent Application (Application Serial No. 16/225,640) was filed on December 19, 2018 as a continuation of PCT/IB2018/0112 and from which U.S. Patent Number 10,407,479 issued on September 10, 2019. The term of the U.S. Patent Number 10,407,479 is September 4, 2038. The issued claims are directed to BIO89-100 and a defined genus specifically encompassing BIO89-100 and compositions thereof (including site-specific mutations at positions 173 and 176), as well as methods for making and using BIO89-100 for a variety of therapeutic indications. Such indications include methods for treating NASH or metabolic syndrome. Subjects wherein there is a need to reduce blood glucose or to reduce HbA1C include those afflicted with diabetes Type 2, NASH and metabolic syndrome. The claims encompass different therapeutic regimens for administering BIO89-100 (e.g., once a week or once every two weeks), which regimens are based on BIO89-100's surprisingly long half-life in vivo.

National phase entry of this PCT Application in March of 2020 provides the opportunity to pursue global protection of specific mutant FGF21 peptide conjugates, and particularly BIO89-100. National phase entry has been initiated in Europe, China, Japan, Australia, Canada, Israel and Korea.

FASN Patents

Our FASN patent portfolio currently consists of three patent families, including patents and/or patent applications in the United States, the European Patent Convention, Canada, Mexico, Israel and Japan.

The first patent family, directed to TEV-48317, which we acquired from Teva under the FASN Agreement, and other 1,4-substituted piperidine-based FASN inhibitors, is currently protected by two granted U.S. patents that cover these compounds, pharmaceutical compositions comprising these compounds, and methods of treating FASN-mediated disorders using these compounds. The non-extended term for these patents would expire on June 17, 2036. A pending U.S. application is directed to additional methods of treatment using these compounds. The second patent family is directed to other 1,4-substituted piperidine-based FASN inhibitors, pharmaceutical compositions, and methods of treating FASN-mediated disorders. The third patent family is directed to spiropiperidine FASN inhibitors, pharmaceutical compositions containing these compounds, and methods of treating FASN-mediated disorders using these compounds.

Employees

As of December 31, 2019, we had 19 full-time employees and 20 total employees. 14 employees are engaged in research and development activities. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Corporate Information

We were incorporated in January 2018 in Israel under the name 89Bio Ltd. 89bio, Inc., the registrant whose name appears on the cover page of this Annual Report on Form 10-K, was incorporated in June 2019 for the purpose of an internal reorganization transaction. In September 2019, all of the equity holders of 89Bio Ltd. exchanged 100% of the equity of 89Bio Ltd. for 100% of the equity of 89bio, Inc. Following this exchange, 89Bio Ltd. became a wholly owned subsidiary of 89bio, Inc.

Our principal executive offices are located at 142 Sansome Street, San Francisco, California 94104 and our telephone number is (415) 500-4614. Our website is *www.89bio.com*. Information contained on or accessible through our website is not a part of this Annual Report on Form 10-K, and the inclusion of our website address in this Annual Report on Form 10-K is an inactive textual reference only.

We file electronically with the SEC our Annual Report 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 Securities Exchange Act of 1934, as amended (the "Exchange Act"). We make available on our website at *www.89bio.com*, under "Investors," free of charge, copies of these reports as soon as reasonably practicable after filing or furnishing these reports with the SEC.

Implications of Being an Emerging Growth Company and a Smaller Reporting Company

We are an emerging growth company ("emerging growth company"), as defined in Section 2(a) of the Securities Act of 1933, as amended (the "Securities Act"), as modified by the Jumpstart Our Business Startups Act of 2012 (the "JOBS Act"), and we may take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including relief from the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended, less extensive disclosure obligations regarding executive compensation in our registration statements, periodic reports and proxy statements, exemptions from the requirements to hold a nonbinding advisory vote on executive compensation, and exemptions from stockholder approval of any golden parachute payments not previously approved. We may also elect to take advantage of other reduced reporting requirements in future filings. As a result, our stockholders may not have access to certain information that they may deem important and the information that we provide to our stockholders may be different than, and not comparable to, information presented by other public reporting companies. We could remain an emerging growth company until the earlier of (1) the last day of the year following the fifth anniversary of the completion of our initial public offering ("IPO"), (2) the last day of the year in which we have total annual gross revenue of at least $1.07 billion, (3) the last day of the year in which we are deemed to be a "large accelerated filer" as defined in Rule 12b-2 under the Exchange Act, which would occur if the market value of our common stock held by non-affiliates exceeded $700.0 million as of the last business day of the second fiscal quarter of such year or (4) the date on which we have issued more than $1.0 billion in non-convertible debt securities during the prior three-year period.

In addition, the JOBS Act also provides that an emerging growth company may take advantage of the extended transition period provided in the Securities Act for complying with new or revised accounting standards. An emerging growth company may therefore delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to avail ourselves of this exemption and, as a result, will not be subject to the same implementation timing for new or revised accounting standards as are required of other public companies that are not emerging growth companies, which may make comparison of our consolidated financial information to those of other public companies more difficult.

We are also a smaller reporting company ("smaller reporting company"), as defined in the Exchange Act. We may continue to be a smaller reporting company even after we are no longer an emerging growth company. We may take advantage of certain of the scaled disclosures available to smaller reporting companies and will be able to take advantage of these scaled disclosures for so long as (i) our voting and non-voting common stock held by non-affiliates is less than $250.0 million measured on the last business day of our second fiscal quarter or (ii) our annual revenue is less than $100.0 million during the most recently completed fiscal year and our voting and non-voting common stock held by non-affiliates is less than $700.0 million measured on the last business day of our second fiscal quarter.

Item 1A. Risk Factors.

An investment in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below before deciding whether to make an investment decision with respect to shares of our common stock. You should also refer to the other information contained in this Annual Report on Form 10-K, including "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our audited consolidated financial statements and related notes. Our business, financial condition, results of operations and prospects could be materially and adversely affected by any of these risks or uncertainties. In any such case, the trading price of our common stock could decline, and you could lose all or part of your investment. We caution you that the risks, uncertainties and other factors referred to below and elsewhere in this Annual Report on Form 10-K may not contain all of the risks, uncertainties and other factors that may affect our future results and operations. Moreover, new risks will emerge from time to time. It is not possible for our management to predict all risks.

Risks Related to Our Business and Industry

We are a clinical-stage biopharmaceutical company with a limited operating history and no products approved for commercial sale. We have incurred net losses since our inception, we expect to incur significant and increasing operating losses and we may never be profitable. Our stock is a highly speculative investment.

We are a clinical-stage biopharmaceutical company with a limited operating history that may make it difficult to evaluate the success of our business to date and to assess our future viability. We commenced operations in 2018, and to date, our operations have been limited to organizing and staffing our company, business planning, raising capital, acquiring our initial product candidate, BIO89-100 and licensing certain related technology, conducting research and development activities, including preclinical studies and early clinical trials, and providing general and administrative support for these operations. 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, we 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. We have limited experience as a company conducting clinical trials and no experience as a company commercializing any products.

We are not profitable and have incurred net losses since our inception. As of December 31, 2019, we had an accumulated deficit of $73.6 million. Consequently, predictions about our future success or viability may not be as accurate as they would be if we had a longer operating history or a history of successfully developing and commercializing pharmaceutical products. We have spent, and expect to continue to spend, significant resources to fund research and development of, and seek regulatory approvals for, BIO89-100 and any future product candidates. We expect to incur substantial and increasing operating losses over the next several years as our research, development, preclinical testing and clinical trial 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. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity (deficit) and working capital. The net losses we incur may fluctuate significantly from quarter-to-quarter such that a period-to-period comparison of our results of operations may not be a good indication of our future performance. 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.

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

BIO89-100 is in the early stages of development. To date, we have not generated any revenue from the licensing or commercialization of BIO89-100. We will not be able to generate product revenue unless and until BIO89-100 or any future product candidate, alone or with future partners, successfully completes clinical trials, receives regulatory approval and is successfully commercialized. As BIO89-100 is in the early stages of development, we do not expect to receive revenue from it for a number of years, if ever. Although we may seek to obtain revenue from collaboration or licensing agreements with third parties, 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 BIO89-100 or any future product candidates also depends on a number of additional factors, including our or our future partners' ability to:

- successfully complete research and clinical development of BIO89-100 and any 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 that supply;
- launch and commercialize future 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 future 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 comparable 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 product candidates 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 will require substantial 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 BIO89-100 or develop new product candidates.

As a clinical-stage biopharmaceutical company, our operations have consumed significant amounts of cash since our inception. We expect our research and development expenses to increase substantially in connection with our ongoing activities, particularly as we conduct our Phase 1b/2a clinical trial and future clinical trials of BIO89-100 and seek regulatory approvals for BIO89-100.

We believe that the net proceeds from our IPO, together with our existing cash and cash equivalents will fund our projected operating requirements into the second half of 2021. 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 and clinical studies for BIO89-100 and any future product candidates we may develop;
- 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 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 of any patents or other intellectual property rights;
- the effect of competing technological and market developments;
- market acceptance of any approved product candidates, including product pricing and product coverage and adequate 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 of BIO89-100; and
- the cost of establishing sales, marketing and distribution capabilities for BIO89-100 and any future product candidates for which we may receive regulatory approval and that we determine to commercialize ourselves or in collaboration with our future partners.

We will require additional capital to discover, develop, obtain regulatory approval for and commercialize BIO89-100 and any future product candidates. We do not have any committed external source of funds. 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. 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 technologies or any product candidates that we otherwise would seek to develop or commercialize ourselves.
- In addition, if BIO89-100 receives approval and is commercialized, we will be required to make milestone and royalty payments to Teva, from whom we acquired certain patents and intellectual property relating to BIO89-100, and from whom we licensed patents and know-how related to glycoPEGylation technology that is used in the manufacture of BIO89-100. For additional information regarding this license agreement, please see the section titled "Business—Agreements with Teva" and Note 5 to our consolidated financial statements accompanying this Annual Report on Form 10-K.

Raising additional capital may cause dilution to existing stockholders, restrict our operations or require us to relinquish rights to our technologies.

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 BIO89-100 and any future product candidates.

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 unable to obtain additional funding on a timely basis, we may be required to curtail or terminate some or all of our development programs or product candidates.

We will need to raise additional funds to operate our business, but additional funds may not be available on acceptable terms, or at all. Any inability to raise required capital when needed could harm our liquidity, financial condition, business, operating results and prospects.

As of December 31, 2019, we had no revenue, an accumulated deficit of $73.6 million and cash and cash equivalents of $93.3 million. Based on our current operating plan, we believe that our cash and cash equivalents, together with the net proceeds from our IPO will be sufficient to meet our anticipated cash requirements into the second half of 2021. However, to date, we have not generated revenues from our activities and have incurred substantial operating losses. We expect that we will continue to generate substantial operating losses for the foreseeable future until we complete development of BIO89-100 or our other product candidates and seek regulatory approvals to market such product candidates. We plan to continue to fund our operations primarily through utilization of our current financial resources and additional raises of capital. We may raise funds from our current investors as well as potential outside investors. We expect to finance future cash needs through public or private equity or debt offerings or product collaborations. However, there is no assurance that such funding will be available to us or that it will be obtained on terms favorable to us or will provide us with sufficient funds to meet our objectives. Any failure to raise capital as and when needed could have a negative impact on our financial condition and on our ability to pursue our business plans and strategies.

Our business depends on the success of BIO89-100, our only product candidate under clinical development, which is in the early stages of clinical development and has not completed a pivotal trial. If we are unable to obtain regulatory approval for and successfully commercialize BIO89-100 or other future product candidates, or we experience significant delays in doing so, our business will be materially harmed.

To date, the primary focus of our product development has been BIO89-100 for the treatment of patients with NASH. Currently, BIO89-100 is our only product candidate under clinical development. This may make an investment in our company riskier than similar companies that have multiple product candidates in active development and that therefore may be able to better sustain a failure of a lead candidate. Successful continued development and ultimate regulatory approval of BIO89-100 for the treatment of NASH or other indications, including SHTG, is critical to the future success of our business. We have invested, and will continue to invest, a significant portion of our time and financial resources in the clinical development of BIO89-100. If we cannot successfully develop, obtain regulatory approval for and commercialize BIO89-100, we may not be able to continue our operations. The future regulatory and commercial success of BIO89-100 is subject to a number of risks, including the following:

- we may not have sufficient financial and other resources to complete the necessary clinical trials for BIO89-100, including, but not limited to, the clinical trials needed to obtain drug approval;
- the mechanism of action of BIO89-100 is complex, and we do not know the degree to which it will translate into a therapeutic benefit, if any, in NASH or any other indication, and we do not know the degree to which the complex mechanism of action may contribute to long-term safety issues or adverse events, if any, when BIO89-100 is taken for prolonged periods such as in the treatment of NASH or any other indication;

- we may not be able to obtain adequate evidence from clinical trials of efficacy and safety for BIO89-100 for the treatment of NASH or other indications;
- in our clinical trials for BIO89-100, we may need to adjust our clinical trial procedures and may need additional clinical trial sites, which could delay our clinical trial progress;
- the results of our clinical trials may not meet the level of statistical or clinical significance required by the FDA or comparable foreign regulatory authorities for marketing approval;
- patients in our clinical trials may suffer serious adverse effects for reasons that may or may not be related to BIO89-100, which could delay or prevent further clinical development;
- the standards implemented by clinical or regulatory agencies may change at any time and we cannot be certain what efficacy endpoints the FDA or foreign clinical or regulatory agencies may require in pivotal clinical trials with respect to NASH or any other indication for the approval of BIO89-100;
- the results of later stage clinical trials may not be as favorable as the results we have observed to date in our preclinical studies and Phase 1a clinical trial;
- if we obtain accelerated approval of BIO89-100 or any other product candidate based on a surrogate endpoint, we may be required to conduct a post-approval clinical outcomes trial to confirm the clinical benefit of the product candidate; if any such post-approval trial is not successful we may not be able to continue marketing the product;
- we cannot be certain of the number and type of clinical trials and non-clinical studies that the FDA or other regulatory agencies will require in order to approve BIO89-100 for the treatment of NASH or any other indication, including SHTG;
- if approved for NASH or SHTG, BIO89-100 will likely compete with products that may reach approval for the treatment of NASH prior to BIO89-100, products that are currently approved for the treatment of SHTG and the off-label use of currently marketed products for NASH and SHTG; and
- we may not be able to obtain, maintain or enforce our patents and other intellectual property rights.

Of the large number of drugs in development in the pharmaceutical industry, only a small percentage results in the submission of a new drug application or a new BLA to the FDA and even fewer are approved for commercialization. Furthermore, even if we do receive regulatory approval to market BIO89-100, any such approval may be subject to limitations on the indicated uses or patient populations for which we may market the products. Accordingly, even if we are able to obtain the requisite financing to continue to fund our development programs, we may be unable to successfully develop or commercialize BIO89-100. If we or any of our future development collaborators are unable to develop, or obtain regulatory approval for, or, if approved, successfully commercialize BIO89-100, we may not be able to generate sufficient revenue to continue our business.

Clinical drug development involves a lengthy and expensive process with uncertain timelines and uncertain outcomes, and the results of prior preclinical or clinical trials are not necessarily predictive of our future results. Our clinical trials may fail to adequately demonstrate the safety and efficacy of BIO89-100 or any future product candidates.

BIO89-100 and any future product candidates will be subject to rigorous and extensive clinical trials and extensive regulatory approval processes implemented by the FDA and comparable foreign regulatory authorities before obtaining marketing approval from these regulatory authorities. The drug development and approval process is lengthy and expensive, and approval is never certain. Investigational new drugs, such as BIO89-100, may not prove to be safe and effective in clinical trials. We have no direct experience as a company in conducting later stage clinical trials required to obtain regulatory approval. We may be unable 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. 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 as a company designing clinical trials, we may be unable to design and execute a clinical trial to support regulatory approval. Even if our current clinical trial is successful, it will be insufficient to demonstrate that BIO89-100 is safe or effective for registration purposes.

There is a high failure rate for drugs and biologic products proceeding through clinical trials. Failure can occur at any time during the clinical trial process. The results of preclinical studies and early clinical trials of BIO89-100 or any future product candidate may not be predictive of the results of later-stage clinical studies or trials and the results of studies or trials in one set of patients or line of treatment may not be predictive of those obtained in another. 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. In addition, data obtained from preclinical and clinical activities is subject to varying interpretations, which may delay, limit or prevent regulatory approval. It is impossible to predict when or if BIO89-100 or any future product candidate will prove effective or safe in humans or will receive regulatory approval. Owing in part to the complexity of biological pathways, BIO89-100 or any future product candidate may 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. The number of patients exposed to product candidates and the average exposure time in the clinical development programs may be inadequate to detect rare adverse events or findings that may only be detected once a product candidate is administered to more patients and for greater periods of time. To date, our Phase 1a clinical trial has involved a small patient population of healthy volunteers and, because of the small sample size in such trial, the results of this clinical trial may be subject to substantial variability and may not be indicative of either future interim results or final results in patients with liver or cardio-metabolic diseases. If we are unable to successfully demonstrate the safety and efficacy of BIO89-100 or other future product candidates and receive the necessary regulatory approvals, our business will be materially harmed.

If we experience delays in clinical testing, our commercial prospects will be adversely affected, our costs may increase and our business may be harmed.

Conducting clinical studies for any product 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 institutional review board at each such site, manufacturing clinical quantities of product candidates and supplying drug product to clinical sites. Currently, we have an active IND with the FDA in the United States for BIO89-100. Because our IND is with the gastrointestinal division of the FDA, we may file an additional IND with another division for any future indications, including SHTG. If any such future IND is not approved by the FDA, our clinical development timeline may be negatively impacted and any future clinical programs may be delayed or terminated.

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 other 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 also could shorten any periods during which we may have the exclusive right to commercialize BIO89-100 and any future product candidates or allow our competitors to bring products to market before we do, which would impair our ability to successfully commercialize BIO89-100 or any future 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 CROs and clinical trial sites;
- ongoing discussions with the FDA or comparable foreign authorities regarding the scope or design of our clinical trials;
- deviations from the trial protocol by clinical trial sites and investigators, or failures to conduct the trial in accordance with regulatory requirements;
- the need to repeat clinical trials as a result of inconclusive or negative results or poorly executed testing or changes in required endpoints or requests for additional information by the FDA or comparable foreign authorities;
- unfavorable FDA inspection and review of a clinical trial site or records of any clinical or preclinical investigation;

- the placement of a clinical hold on a clinical trial by the FDA or comparable foreign authorities;
- delays in obtaining, or the inability to obtain, required approvals from institutional review boards or other governing entities at clinical sites selected for participation in our clinical trials;
- 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 to the clinical sites;
- insufficient supply or deficient quality of product candidate materials or other materials necessary to conduct our clinical trials;
- 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;
- delays in enrolling participants into our clinical trials;
- delays in patients completing a trial or returning for post-treatment follow-up;
- delays caused by patients dropping out of a trial due to side effects, disease progression or otherwise;
- serious and unexpected drug-related adverse effects experienced by participants in our clinical trials;
- implementation of new, or changes to, guidance or interpretations from the FDA or comparable foreign authorities with respect to approval pathways for any product candidates we are pursuing, such as the draft guidance documents from the FDA and the European Medicines Agency for the development of NASH that were issued in 2018 and 2019;
- withdrawal of clinical trial sites from our clinical trials 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 future collaborators' inability to timely complete clinical development could result in additional costs to us as well as impair our ability to generate product revenue, continue development, commercialize BIO89-100 and any future product candidates, reach sales milestone payments and receive royalties on product sales. In addition, if we make changes to a product candidate, we may need to conduct additional nonclinical studies or clinical trials to bridge or demonstrate the comparability of our modified product candidate to earlier versions, which could delay our clinical development plan or marketing approval for our current product candidate and any future product candidates.

If we encounter difficulties in enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

The timely completion of clinical trials largely depends on patient enrollment. We may encounter delays in enrolling, or be unable to enroll, a sufficient number of patients to complete any of our clinical trials, and even once enrolled, we may be unable to retain a sufficient number of patients to complete any of our trials.

Furthermore, as a result of the inherent difficulties in diagnosing NASH, which can currently only be definitively diagnosed through a liver biopsy, and the significant competition for recruiting NASH patients in clinical trials, we or our future collaborators may be unable to enroll the patients we need to complete clinical trials on a timely basis, or at all.

Many factors affect patient enrollment, including:

- the size and nature of the patient population, which may be limited due to diagnostic requirements;
- the number and location of clinical sites;
- competition with other companies for clinical sites or patients;
- the availability and amount of any patient stipend;

- the eligibility and exclusion criteria for the trial, including any potential requirement for a biopsy;
- the design of the clinical trial;
- inability to obtain and maintain patient consents;
- significant adverse events or other side effects observed, if any;
- 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 (oral versus injectables, like BIO89-100), including any new drugs that may be approved for the indications we are investigating.

In addition, our competitors, some of whom have significantly greater resources than we do, are conducting clinical trials for the same indications and seek to enroll patients in their studies that may otherwise be eligible for our clinical studies or trials, which could lead to slow recruitment and delays in our clinical programs. Further, since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which could further reduce the number of patients who are available for our clinical trials in these sites.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. If we are unable to enroll a sufficient number of patients that will complete clinical testing, we will be unable to seek or gain marketing approval for BIO89-100 and any future product candidates and our business will be harmed. Even if we are able to enroll a sufficient number of patients in our clinical studies or trials, delays in patient enrollment may result in increased costs or may affect the timing or outcome of our clinical trials, which could prevent completion of these trials and adversely affect our ability to advance the development of BIO89-100 and any future product candidates.

An epidemic of the coronavirus disease is ongoing and may result in significant disruptions to our clinical trials or other business operations, which could have a material adverse effect on our business.

An epidemic of the coronavirus disease is ongoing throughout the world. As the outbreak is still evolving, much of its impact remains unknown. As of this filing, it is impossible to predict the effect and potential spread of the coronavirus disease globally. The coronavirus disease may cause significant disruptions to our clinical trials. If the patients involved with our clinical trials become infected with the coronavirus disease, we may have more AEs and deaths in our clinical trials as a result. We may also face difficulties enrolling patients in our clinical trials if the patient populations that are eligible for our clinical trials are impacted by the coronavirus disease. Additionally, if our clinical trial patients are unable to travel to our clinical trial sites as a result of quarantines or other restrictions resulting from the coronavirus disease, we may experience higher drop-out rates or delays in our clinical trials, and some patients may not be able to comply with clinical trial protocols if quarantines impede patient movement or interrupt healthcare services, which could impact our ability to determine the efficacy or safety of BIO89-100. Site initiation and patient enrollment may also be delayed due to prioritization of hospital resources toward the COVID-19 outbreak.

Additionally, travel restrictions have been implemented with respect to certain countries in an effort to contain the coronavirus disease, and several countries have expanded screenings of travelers. As travel restrictions are increasingly implemented and extended to other countries, we and our CROs may be unable to visit our clinical trial sites and monitor the data from our clinical trials on timely basis. Our employees may also face travel restrictions, which would impact our business. Furthermore, some of our manufacturers and suppliers are in Europe and may be impacted by port closures and other restrictions resulting from the coronavirus outbreak, which may disrupt our supply chain or limit our ability to obtain sufficient materials for our drug products.

The ultimate impact of the COVID-19 outbreak 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, our CROs, healthcare systems or the global economy as a whole. However, any one or a combination of these events could have an adverse effect on the operation of and results from our clinical trials and on our other business operations, which could prevent or delay us from obtaining approval for BIO89-100.

We are initially developing BIO89-100 for the treatment of NASH, an indication for which there are no approved products. This makes it difficult to predict the timing and costs of the clinical development of BIO89-100 for the treatment of NASH.

Our current research and development efforts are focused on developing BIO89-100 for the treatment of NASH, an indication for which there are no approved products. The regulatory approval process for novel product candidates such as BIO89-100 can be more expensive and take longer than for other, better known or extensively studied product candidates. As other companies are in later stages of clinical trials for their potential NASH therapies, we expect that the path for regulatory approval for NASH therapies may continue to evolve in the near term as these other companies refine their regulatory approval strategies and interact with regulatory authorities. Such evolution may impact our future clinical trial designs, including trial size and endpoints, in ways that we cannot predict today. Our anticipated development costs would likely increase if development of BIO89-100 or any future product candidate is delayed because we are required by the FDA to perform studies or trials in addition to, or different from, those that we currently anticipate. Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to predict the timing or amount of any increase in our anticipated development costs.

BIO89-100 and any future 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 BIO89-100 or any future 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 studies may be required to evaluate the safety profile of BIO89-100 or any future product candidates.

While no serious adverse events were reported in our Phase 1a clinical trial of BIO89-100, the following treatment-related adverse events were reported in at least two subjects in the treatment cohort: injection site reactions and headaches. Further, it is possible that side effects will become apparent in long-term animal safety studies, such as those that remain ongoing. We have seen evidence of physiological changes in mice that are consistent with the changes that may accompany a dramatic amount of weight loss relative to growth in non-obese animals. As with any animal safety finding, to the extent that these side effects are determined to be clinically relevant, they could have a negative impact on our clinical program.

Future results of our trials could reveal a high and unacceptable severity and prevalence of side effects 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 BIO89-100 or any future 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, results of operations and prospects.

It may be difficult to discern whether certain events or symptoms observed during our clinical trials or by patients using our approved products are related to BIO89-100 or any future product candidates or approved products or some other factor. As a result, we and our development programs may be negatively affected even if such events or symptoms are ultimately determined to be unlikely related to BIO89-100 or any future product candidates or approved products. We cannot assure you that additional or more severe adverse side effects related to BIO89-100 or any future product candidates will not be observed in our clinical trials or in the commercial setting. Further, we expect that BIO89-100 will require multiple administrations vis subcutaneous injection in the course of a clinical trial, and this chronic administration increases the risk that our clinical drug development programs may not uncover all possible adverse events that may eventually be experienced by patients treated with BIO89-100, such as rare adverse events or chance findings that may only be detected once product candidates are administered to ore patients or for greater periods of time. If observed, such adverse side effects could delay or preclude regulatory approval of BIO89-100 or any future product candidates, limit commercial use or result in the withdrawal of previously granted marketing approvals. If we or others identify undesirable or unacceptable side effects caused by BIO89-100 or any future product candidates or products:

- we may be required to modify, suspend or terminate our clinical trials;
- we may be required to modify or include additional dosage and administration instructions, warnings and precautions, contraindications, boxed warnings, limitations, restrictions or other statements in the product label for our approved products, or issue field alerts to physicians and pharmacies;

- we may be required to conduct costly additional clinical trials;
- we may be subject to limitations on how we may promote our approved products;
- sales of our approved products may decrease significantly;
- regulatory authorities may require us to take our approved products off the market;
- we may be subject to regulatory investigations, government enforcement actions, litigation or product liability claims; and
- our products may become less competitive or our reputation may suffer.

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.

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

The biopharmaceutical industry is intensely competitive and subject to rapid innovation and significant technological advancements. We believe the key competitive factors that will affect the development and commercial success of BIO89-100 and any future product candidates are efficacy, safety and tolerability profile, reliability, convenience of dosing, price, the level of generic competition and reimbursement. Our competitors include multinational pharmaceutical companies, specialized biotechnology companies, universities and other research institutions. A number of biotechnology and pharmaceutical companies are pursuing the development or marketing of pharmaceuticals that target the same diseases that we are targeting. Smaller or earlier-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. Given the high incidence of NASH and SHTG, it is likely that the number of companies seeking to develop products and therapies for the treatment of liver and cardio-metabolic diseases, such as NASH and SHTG, will increase.

There are no currently approved therapies for the treatment of NASH. Although there are no approved therapies that specifically target the signaling pathways that BIO89-100 is designed to affect, there are numerous currently approved therapies for treating diseases other than NASH and some of these currently approved therapies may exert effects that could be similar to BIO89-100. 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 BIO89-100 or any future 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 BIO89-100 or any future product candidates progress through clinical development. In addition, to the extent BIO89-100 or any future product candidates are approved for cardio-metabolic indications, such as SHTG, the commercial success of our products will also depend on our ability to demonstrate benefits over the then-prevailing standard of care, including diet, exercise and lifestyle modifications.

Further, if BIO89-100 or any future product candidates are approved for the treatment of SHTG, we will compete with currently approved therapies and therapies further along in development. Our competitors both in the United States and abroad include large, well-established pharmaceutical and generic companies with significantly greater name recognition. Our competitors may be able to charge lower prices than we can, which may adversely affect our market acceptance. Many of these competitors have greater resources than we do, including financial, product development, marketing, personnel and other resources. Clinical trials for the treatment of SHTG may be relatively costly and time consuming. The requirements for approval by the FDA and comparable foreign regulatory authorities may change over time and this may require changes to ongoing or future clinical trial designs that could impact timelines and cost.

If our competitors market products that are more effective, safer or cheaper than our products or that reach the market sooner than our products, we may not achieve commercial success. In addition, the biopharmaceutical industry is characterized by rapid technological change. Because our research approach integrates many technologies, it may be difficult for us to stay abreast of the rapid changes in other technologies. If we fail to stay at the forefront of technological change, we may be unable to compete effectively.

Technological advances or products developed by our competitors may render our technologies, products or product candidates obsolete, less competitive or not economical.

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 longer operating histories and greater experience than we have in undertaking nonclinical studies and human clinical trials of new pharmaceutical products and in obtaining regulatory approvals of human therapeutic products. Many of our competitors have established distribution channels for 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.

As a result, our competitors may obtain regulatory approval of their products more rapidly than we do or may obtain patent protection or other intellectual property rights that limit our ability to develop or commercialize our product candidate or any future product candidates. Our competitors may also develop and succeed in obtaining approval for 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 we are 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 candidate or any future 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 enrolling patients for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs. Our inability to compete effectively in any of these aspects of our business could harm our business, financial condition, results of operations and prospects.

Lack of efficacy, adverse events or undesirable side effects may emerge in clinical trials conducted by third parties developing FGF product candidates, which could adversely affect our stock price, our ability to attract additional capital and our development program.

Lack of efficacy, adverse events or undesirable side effects may emerge in clinical trials conducted by third parties developing FGF product candidates like ours. For example, Bristol-Myers Squibb Company and Akero Therapeutics, Inc. are also developing FGF21 product candidates for the treatment of NASH. We have no control over their clinical trials or development program, and lack of efficacy, adverse events or undesirable side effects experienced by subjects in their clinical trials could adversely affect our stock price, our ability to attract additional capital and our development of BIO89-100 or even the viability of BIO89-100 as a product candidate, including by creating a negative perception of FGF therapeutics by healthcare providers or patients.

Interim, topline and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may publicly disclose preliminary or topline data from our clinical trials, which are based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the topline results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Topline data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, topline data should be viewed with caution until the final data are available. From time to time, we may also disclose interim data from our clinical trials. In addition, we may report interim analyses of only certain endpoints rather than all endpoints. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available.

In addition, adverse changes between interim data and final data could significantly harm our business and prospects. Additional disclosure of interim data by us or by our competitors in the future could also result in volatility in the price of our common stock. Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular drug, drug candidate or our business. If the topline data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, BIO89-100 or any future product candidates may be harmed, which could harm our business, financial condition, results of operations and prospects.

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

We are in the early stages of building the full management team and employee base that we anticipate we will need to complete the development BIO89-100 and other future product candidates. As of December 31, 2019, we had 20 employees, some of whom are based in the United States and some of whom are based in Israel. As we advance our preclinical and clinical development programs for product candidates, seek regulatory approval in the United States and elsewhere and increase the number of ongoing product development programs, we anticipate that we will need to increase our product development, scientific and administrative headcount. We will also need to establish commercial capabilities in order to commercialize any product candidates that may be approved. Such an evolution may impact our strategic focus and our deployment and allocation of resources. Our management, personnel and systems may experience difficulty in adjusting to our growth and strategic focus.

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 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 execute our business strategies and may be forced to expend more resources than anticipated addressing these issues.

We may acquire additional technology 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 technologies, 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.

In addition, in order to continue to meet our obligations as a public company and to support our anticipated long-term growth, we will need to increase our general and administrative capabilities. Our management, personnel and systems may not be adequate to support this future growth.

If we are unable to successfully manage our growth and the increased complexity of our operations, our business, financial position, results of operations and prospects may be materially and adversely affected.

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

We may not be able to attract or retain qualified personnel and consultants due to the intense competition for such individuals among in the biotechnology and pharmaceutical industries. If we are not able to attract and retain necessary personnel and consultants to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development and commercial objectives, our ability to raise additional capital and our ability to implement our business strategy.

Our industry has experienced a high rate of turnover of management personnel in recent years. We are highly dependent on the development, regulatory, commercialization and business development expertise of the members of our executive team, as well as other key employees and consultants. If we lose one or more of our executive officers or other key employees or consultants, our ability to implement our business strategy successfully could be seriously harmed. Any of our executive officers or other key employees or consultants may terminate their employment at any time and replacing such individuals may be difficult and time-consuming because of the limited number of individuals in our industry with the necessary breadth of skills and experience. Competition to hire and retain employees and consultants from this limited pool is intense, and we may be unable to hire, train, retain or motivate such individuals. Additionally, we do not currently maintain "key person" life insurance on the lives of our executives or any of our employees. This lack of insurance means that we may not receive adequate compensation for the loss of the services of these individuals. 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.

We have relied on, and expect to continue to rely on, third-party manufacturers to produce BIO89-100 or any future product candidates. Any failure by a third-party manufacturer to produce acceptable product candidates for us pursuant to our specifications and regulatory standards may delay or impair our ability to initiate or complete our clinical trials, obtain and maintain regulatory approvals or commercialize approved products.

The manufacturing of biologic drugs such as BIO89-100 is complex and the process of identifying the qualifying suppliers takes a significant investment of time and money. We do not own or operate manufacturing facilities for the production of clinical or commercial quantities of our product candidates, and we lack the resources and the capabilities to do so. As a result, we currently rely, and expect to rely for the foreseeable future, on third-party manufacturers to supply us with BIO89-100 and any future product candidates.

We currently have a sole source relationship with Northway Biotechpharma ("BTPH") pursuant to which they supply us with BIO89-100. If there should be any disruption in our supply arrangement with BTPH, including any adverse events affecting BTPH, it could have a negative effect on the clinical development of BIO89-100 and other operations while we work to identify and qualify an alternate supply source.

We do not have a long-term supply agreement with any third-party manufacturer. Reliance on third-party manufacturers entails risks to which we would not be subject if we manufacture product candidates or products ourselves. For example, if we do not maintain our key manufacturing relationships, we may fail to find replacement manufacturers or develop our own manufacturing capabilities in a timely manner or at all, which could delay or impair our ability to obtain regulatory approval for our products and substantially increase our costs or deplete profit margins, if any. If we do find replacement manufacturers, we may not be able to enter into agreements with them on terms and conditions favorable to us, and there could be a substantial delay before new facilities could be qualified and registered with the FDA and other comparable foreign regulatory authorities.

Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

- the possible failure of the third party to manufacture product candidates according to our schedule, or at all, including if our third-party contractors give greater priority to the supply of other products over our product candidates or otherwise do not satisfactorily perform according to the terms of the agreements between us and them;
- the possible breach of the manufacturing agreement by the third party because of factors beyond our control (including a failure to manufacture product candidates in accordance with our product specifications);
- the possible mislabeling of clinical supplies, potentially resulting in the wrong dose amounts being supplied or active drug or placebo not being properly identified;
- the possibility of clinical supplies not being delivered to clinical sites on time, leading to clinical trial interruptions, or of drug supplies not being distributed to commercial vendors in a timely manner, resulting in lost sales;

- the possible misappropriation of our proprietary information, including our trade secrets and know-how;
- 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.

Certain raw materials necessary for the manufacture of BIO89-100 under our current manufacturing process, such as reagents that are needed for the glycoPEGylation, are available only from a single supplier. In April 2018, we entered into a Reagent Supply and Technology Transfer Agreement with Teva under which Teva agreed to supply us several reagents required for the glycoPEGylation process until December 31, 2022 and transfer the know-how required for our production of these reagents. We expect the manufacture of these reagents will be transferred to a new supplier prior to expiration of the agreement with Teva. Any complications arising under our agreement with Teva, with the subsequent transfer of know-how to us, or any difficulties securing a new supplier could considerably delay the manufacture of BIO89-100. Any significant delay in the acquisition or decrease in the availability of these raw materials from Teva or any new supplier could considerably delay the manufacture of BIO89-100, which could adversely impact the timing of any planned trials or the regulatory approvals of BIO89-100.

The FDA and other comparable foreign regulatory authorities require manufacturers to register manufacturing facilities. The FDA and other comparable foreign regulatory authorities also inspect these facilities to confirm compliance with current good manufacturing practices ("cGMP"). Contract manufacturers may face manufacturing or quality control problems causing drug substance production and shipment delays or a situation where the contractor may not be able to maintain compliance with the applicable cGMP requirements. We may have little to no control regarding the occurrence of third-party manufacturer incidents. Any failure to comply with cGMP requirements or other FDA or comparable foreign regulatory requirements could adversely affect our clinical research activities and our ability to develop BIO89-100 or any future product candidates and market our products following approval. Our sole source supplier, BTPH, has not yet manufactured a commercial product, and as a result, has not been subject to inspection by the FDA and other comparable foreign regulatory authorities.

If BIO89-100 or any future product candidates are approved by the FDA or other comparable foreign regulatory authorities for commercial sale, we may need to manufacture such product candidate in larger quantities. We intend to use third-party manufacturers for commercial quantities of BIO89-100 to the extent we advance this product candidate and other product candidates. Our 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 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.

In addition, the operations of our third-party manufacturers may be subject to earthquakes, power shortages, telecommunications failures, failures or breaches of information technology systems, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics, and other natural or man-made disasters or business interruptions. Damage or extended periods of interruption to our facilities due to fire, natural disaster, power loss, communications failure, unauthorized entry or other events could cause us to cease or delay development of some or all of our product candidates. Our ability to obtain clinical supplies of our product candidates could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption.

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

In some cases, the technical skills or technology required to manufacture our product candidates may be unique or proprietary to the original manufacturer, we may have difficulty transferring such skills or technology to another third party and a feasible alternative many not exist. These factors would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to have another third party manufacture our product candidates. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines. For example, in the event that we need to switch our third-party manufacturer of BIO89-100 from BTPH, which is our sole manufacturing source for BIO89-100, we anticipate that the complexity of the glycoPEGylation manufacturing process may materially impact the amount of time it may take to secure a replacement manufacturer. The delays associated with the verification of a new manufacturer, if we are able to identify an alternative source, could negatively affect our ability to develop product candidates in a timely manner or within budget.

The manufacture of biologic products is complex and we are subject to many manufacturing risks, any of which could substantially increase our costs and limit supply of our products.

To date, BIO89-100 has been manufactured by a single third-party manufacturer, BTPH, solely for preclinical studies and clinical trials. This manufacturer may not be able to scale production to the larger quantities required for large clinical trials and to commercialize BIO89-100. The process of manufacturing BIO89-100 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;
- 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.

The manufacture of biologic products, and in particular, the glycoPEGylation process, 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 BIO89-100 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 human clinical trials or commercialization. Any delay or interruption in the supply of clinical trial materials, including as a result of breach by us or BTPH of our agreement with BTPH, or our inability to agree to the terms of supply or related services in any statement of work, 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.

We plan to develop a new drug product formulation for BIO89-100 and we may be unsuccessful. Any changes in methods of product candidate manufacturing or formulation may result in the need to perform new clinical trials, which would require additional costs and cause delay.

We plan to develop a new drug product formulation of BIO89-100 for late stage clinical trials and commercialization. Our current drug product is stored as a frozen liquid and is therefore not well-suited to larger clinical trials or commercialization. We have engaged a formulation development company to explore both a new refrigerated liquid formulation and a freeze-dried, or lyophilized formulation. We also plan to begin development of a pen-type autoinjector for the new drug product formulation. There is no assurance that we will be successful in developing a new drug product formulation or an autoinjector on a timely basis or at all, which could impede our development and commercialization strategy for BIO89-100. The FDA or other comparable foreign regulatory authorities could require nonclinical studies or clinical trials to support introduction of any new formulation and autoinjector, which could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase our clinical trial costs, delay approval of BIO89-100 and jeopardize our ability to commence product sales and generate revenue from BIO89-100, if approved.

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 current Good Clinical Practices, 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 BIO89-100 or any future 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 other 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, marketing approval and/or commercialization of BIO89-100 or any future product candidates, producing additional losses and depriving us of potential revenue.

In addition, while we have received the majority of the knowledge with regard to our current product candidate from Teva, we may still depend on Teva to provide information and documentation regarding certain aspects of BIO89-100 or any future product candidates. If Teva delays providing or fails to provide such information or documentation, we may also be delayed in our efforts to successfully commercialize BIO89-100 or any future product candidates. We also depend on Teva to support our efforts to transfer the manufacturing process to a contract manufacturer. If Teva is unable to or otherwise fails to support such transfer, we may incur significant delay and increased costs in commercializing BIO89-100 or any future product candidates.

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.

We expect to depend on collaborators, partners, licensees, clinical investigators, CROs, 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 substance and drug product and to market, sell and distribute any products we successfully develop. Any problems we experience with any of these third parties could delay the development, commercialization and manufacturing of our product candidates, which could harm our results of operations.

We cannot guarantee that we will be able to successfully negotiate agreements for, or maintain relationships with, collaborators, partners, licensees, clinical investigators, CROs, manufacturers and other third parties on favorable terms, if at all. If we are unable to obtain or maintain these agreements, we may not be able to clinically develop, formulate, manufacture, obtain regulatory approvals for or commercialize BIO89-100 and any future product candidates, which will in turn adversely affect our business.

We expect to expend substantial management time and effort to enter into relationships with third parties and, if we successfully enter into such relationships, to manage these relationships. In addition, substantial amounts will be paid to third parties in these relationships. However, we cannot control the amount or timing of resources our future 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, while we manage the relationships with third parties, we cannot control all of the operations of and any outsourcing used by such third parties. We rely on third parties' knowledge regarding specific local laws and regulatory requirements in foreign jurisdictions, where applicable.

If we fail to develop and commercialize additional product candidates, we may be unable to grow our business.

Although the development and commercialization of BIO89-100 is currently our primary focus, as part of our longer-term growth strategy, we plan to evaluate the development and commercialization of other therapies related to NASH and other liver and cardio-metabolic diseases. The success of this strategy depends primarily upon our ability to identify and validate new therapeutic candidates, and to identify, develop and commercialize new drugs and biologics. Our research efforts may initially show promise in discovering potential new drugs and biologics, yet fail to yield product candidates for clinical development for a number of reasons, including:

- we may need to rely on third parties to generate molecules 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 our product candidates unmarketable;
- product candidates may cause adverse effects in patients or subjects, even after successful initial toxicology studies, which may make the product candidates unmarketable;
- product candidates may not demonstrate a meaningful benefit to patients or subjects; and
- our future collaboration partners may change their development profiles or plans for potential product candidates or abandon a therapeutic area or the development of a 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. Future research programs to identify new product candidates may require substantial technical, financial and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful.

Product candidates may require additional, time-consuming development efforts prior to commercial sale, including preclinical studies, clinical trials and approval by the FDA and/or comparable foreign regulatory authorities. All product candidates are prone to the risks of failure that are inherent in pharmaceutical product development, including the possibility that the product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities. In addition, we cannot assure you that any such products that are approved will be manufactured or produced economically, be successfully commercialized, be widely accepted in the marketplace, or be more effective than other commercially available alternatives.

We may use our limited financial and human resources to pursue a particular research program or product candidate that is ultimately unsuccessful or less successful than other programs or product candidates that we may have forgone or delayed.

Because we have limited personnel and financial resources, we may forego or delay the development of certain programs or product candidates that later prove to have greater commercial potential than the programs or product candidates that we do pursue. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs for product candidates may not yield any commercially viable products. Similarly, our decisions to delay or terminate drug development programs may also be incorrect and could cause us to miss valuable opportunities. If we fail to accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through strategic collaboration, licensing or other arrangements or we may allocate our limited internal resources to that product candidate when it would have been more advantageous to enter into such an arrangement. Any such failure could have a material adverse effect on our business, financial condition, results of operations or prospects.

As we evolve from a company that is primarily involved in clinical development to a company that is also involved in commercialization, we may encounter difficulties in expanding our operations successfully.

As we advance our product candidates through clinical trials, we will need to expand our development, regulatory, manufacturing, and marketing and sales capabilities and may need to further contract with third parties to provide these capabilities, such as collaborators, distributors, marketers and additional suppliers. We currently have no experience as a company in or infrastructure for sales, marketing and distribution, and our operations are currently limited to clinical development activities and as our operations expand, we likely will need to manage additional relationships with such third parties.

If BIO89-100 or any future product candidate is approved, we intend either to establish a sales organization with technical expertise and supporting distribution capabilities to commercialize BIO89-100 or any future product candidate or to outsource such functions to one or more third parties. Either of these options would be expensive and time-consuming. Some or all of these costs may be incurred in advance of any approval of BIO89-100 or any future product candidate. In addition, we may not be able to hire a sales force that is sufficient in size or has adequate expertise in the medical markets that we intend to target. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely affect the commercialization of BIO89-100 and other future product candidates.

Maintaining third-party relationships for these purposes will impose significant added responsibilities on members of our management and other personnel. We must be able to effectively manage our development efforts, recruit and train sales and marketing personnel, effectively manage our participation in the clinical trials in which our product candidates are involved and improve our managerial, development, operational and finance systems, all of which may impose a strain on our administrative and operational infrastructure.

If we enter into arrangements with third parties to perform sales, marketing or distribution services, any product revenues that we receive, or the profitability of these product revenues to us, are likely to be lower than if we were to market and sell any products that we develop without the involvement of these third parties. In addition, we may not be successful in entering into arrangements with third parties to sell and market our products or in doing so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our products.

We may seek to establish commercial collaborations for our product candidates, 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. We may decide to collaborate with other pharmaceutical and biotechnology companies for the development and potential commercialization of our product candidates.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator’s resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator’s evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or comparable foreign regulatory authorities, 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 technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborators may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate.

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 may not be successful in our efforts to identify, in-license or acquire, discover, develop or commercialize additional product candidates.

Although a substantial amount of our effort will focus on the development and potential commercialization of BIO89-100, we also may seek to identify, in-license or acquire, discover, develop and commercialize additional product candidates. We cannot assure you that our effort to in-license or acquire additional product candidates will be successful. Even if we are successful in in-licensing or acquiring additional product candidates, their requisite development activities may require substantial resources, and we cannot assure you that these development activities will result in regulatory approvals.

BIO89-100 and any future 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 and others in the medical community. Given the number of drugs in development for the treatment of NASH, if we are unsuccessful in achieving a differentiated profile with BIO89-100 based on efficacy, safety and tolerability, dosing and administration, market acceptance will be limited. Efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources and may not be successful. 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 countries or regions 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. This may be particularly true for drugs that treat NASH or SHTG, which some healthcare providers and payors may deem to be a “lifestyle” disease that could be ameliorated by changes in diet and exercise. The degree of market acceptance of any of our approved product candidates will depend on a number of factors, including:

- the efficacy, safety and dosing 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 physicians 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, including any requirements for biopsy-proven NASH prior to being approved for reimbursement;
- patients' willingness to pay out-of-pocket in the absence of coverage and/or adequate reimbursement from third-party payors;
- 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 BIO89-100 or any future product candidate, we may face challenges to achieving profitability such as our products becoming 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 third-party payors, including government health care programs and private health insurers. Such third-party payors 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. 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 future collaborators 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 future collaborators obtain marketing approval. If coverage and reimbursement are not available or reimbursement is available only to limited levels, we and our future collaborators 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 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.

To become and remain profitable, we or any potential future collaborator must develop and eventually commercialize BIO89-100 or any future product candidates with significant market potential at an adequate profit margin after cost of goods sold and other expenses. Commercialization of BIO89-100 or any future product candidates may entail a substantial cost of goods sold and there can be no assurance that we will be able to achieve a suitable gross margin with respect to sales of BIO89-100 or any future product candidates.

Healthcare reform in the United States may negatively impact our ability to profitably sell our product candidates, if approved, and to recoup the upfront investment needed to obtain regulatory approval of our product candidates.

Third-party payors, whether domestic or foreign, or governmental or commercial, are continually developing and advancing new 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 Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the "Affordable Care Act") was enacted, which includes measures that have significantly changed the way health care is financed by both governmental and private insurers. Among the provisions of the Affordable Care Act of particular importance include:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, which is apportioned among these entities according to their market share in certain government healthcare programs;
- a Medicare Part D coverage gap discount program, in which manufacturers must agree to offer point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13.0% of the average manufacturer price for branded and generic drugs, respectively;
- a 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;
- a licensure framework for follow-on biologic products;
- an extension of a manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in and conduct comparative clinical effectiveness research, along with funding for such research; and
- establishment of a Center for Medicare Innovation at the Centers for Medicare & Medicaid Services ("CMS") to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

There remain judicial, executive, and congressional challenges to certain aspects of the Affordable Care Act which could potentially void or significantly modify the Affordable Care Act in part or in whole. For example, since January 2017, President Trump signed Executive Orders and other directives designed to delay, circumvent, or loosen certain requirements mandated by the Affordable Care Act. On December 22, 2017, President Trump signed into law the Tax Act, which includes a provision repealing the individual mandate to maintain health insurance coverage under the Affordable Care Act effective January 1, 2019. Additionally, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the Affordable Care Act's mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminates the health insurer tax. On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas ruled that the individual mandate is a critical and inseverable feature of the Affordable Care Act, and because it was repealed as part of the Tax Act, the remaining provisions of the Affordable Care Act are invalid as well. The decision was been appealed to the United States Court of Appeals for the Fifth Circuit and on December 18, 2019, the United States Court of Appeals for the Fifth Circuit upheld the District Court's ruling that the individual mandate was unconstitutional, but remanded the case back to the District Court to determine whether the remaining provisions of the Affordable Care Act were nonetheless valid. On March 2, 2020, the United States Supreme Court granted the petitions for writs of certiorari to review this case, and has allotted one hour for oral arguments, which are expected to occur in the fall. It is unclear how such litigation and other efforts will impact the Affordable Care Act.

At the same time, there has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. congressional inquiries and proposed bills designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies for drugs. At the federal level, the Trump administration's budget proposal for the government's fiscal year 2021 includes a $135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. The Trump administration previously released a "Blueprint," or plan, to lower drug prices and reduce out of pocket costs of drugs that contained 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 in 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 product 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. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate product 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, including our ability to recoup the upfront investment needed to obtain regulatory approval for our 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 use of our international facilities subject us to U.S. and foreign governmental trade, import and export, and customs regulations and laws. Compliance with these regulations and laws is costly and exposes us to penalties for non-compliance. Furthermore, if we succeed in developing any products, we intend to market them in other jurisdictions in addition to the United States. If approved, we may hire sales representatives and conduct physician and patient association outreach activities outside of the United States.

Doing business internationally potentially involves a number of risks, including but not limited to:

- multiple, conflicting and changing laws and regulations such as privacy regulations, tax laws, export and import restrictions, employment laws, regulatory requirements, and other governmental approvals, permits and licenses;
- failure by us to obtain and maintain regulatory approvals for the use of our products in various countries;
- rejection or qualification of foreign clinical trial data by the competent authorities of other countries;

- 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;
- a shortage of high-quality employees;
- laws and business practices favoring local companies;
- 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, actual or potential public health emergencies, including the recent coronavirus (COVID-19) disease outbreak, boycotts, curtailment of trade and other business restrictions;
- the imposition of restrictions on the activities of foreign agents and representatives;
- 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.

If we fail to comply with foreign regulatory requirements governing human clinical trials and marketing approval for drugs, we could be prevented from selling our product candidates in foreign markets, which may adversely affect our operating results and financial condition.

The requirements governing the conduct of clinical trials, product licensing, pricing, and reimbursement for marketing our product candidates outside the United States vary greatly from country to country and may require additional testing. We expect that our future clinical development of our product candidates will involve a number of clinical trials in foreign jurisdictions. We have no direct experience as a company in obtaining foreign regulatory approvals. The time required to obtain approvals outside the United States may differ from that required to obtain FDA approval. We may not obtain foreign regulatory approvals on a timely basis, if at all. Approval by the FDA does not guarantee approval by comparable foreign regulatory authorities, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other countries or by the FDA. Failure to comply with these regulatory requirements or obtain required approvals could impair our ability to develop foreign markets for our product candidates and may have a material adverse effect on our results of operations and financial condition.

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 commercialize any resulting products. Product liability claims may be brought against us by subjects enrolled in our clinical trials, patients, or others using 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;
- product recalls or a change in the indications for which products may be used;

- 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 employees, contractors, vendors, principal investigators, consultants and future partners may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of fraud or other misconduct by our employees, contractors, vendors, principal investigators, consultants or future partners. Misconduct by these parties could include failures to comply with FDA regulations, to provide accurate information to the FDA, to comply with federal and state healthcare fraud and abuse laws and regulations, to report financial information or data timely, completely or accurately, or to disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Third-party misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. Although we have adopted a Code of Business Conduct and Ethics, it is not always possible to identify and deter misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us resulting from this misconduct and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions. If we or our future partners market products in a manner that violates fraud and abuse and other healthcare laws, or if we or our future partners violate government price reporting laws, we or our future partners may be subject to administrative civil and/or criminal penalties, among other sanctions.

Most states also have statutes or regulations similar to these federal laws, which may apply to items such as pharmaceutical products and services reimbursed by private insurers. We and/or our future partners may be subject to administrative, civil and criminal sanctions for violations of any of these federal and state laws.

Pharmaceutical and other healthcare companies have been prosecuted under these laws for a variety of promotional and marketing activities, such as: providing free trips, free goods, sham consulting fees and grants and other monetary benefits to prescribers; reporting to pricing services inflated average wholesale prices that were then used by federal programs to set reimbursement rates; engaging in off-label promotion; and submitting inflated best price information to the Medicaid Rebate Program to reduce liability for Medicaid rebates. Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations.

Our business operations and relationships with investigators, healthcare professionals, consultants, third-party payors, patient organizations and customers are subject to broadly applicable healthcare regulatory laws, which could expose us to penalties.

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any product candidate for which we obtain regulatory approval. Our current and future arrangements may expose us to broadly applicable fraud and abuse and other healthcare laws that may constrain the business or financial arrangements and relationships through which we would research, market, sell and distribute our products. Even though we will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors, federal and state healthcare laws pertaining to fraud and abuse are and will be applicable to our business. Such laws include, but are not limited to, the following:

- Federal false claims laws, including the federal civil False Claims Act ("FCA"), which can be enforced through civil whistleblower or qui tam actions, and false statements and civil monetary penalties law prohibit, among others, any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government or knowingly making, or causing to be made, a false statement to get a false claim paid.
- The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce, or in return for, purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid or other federally financed healthcare programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers, on the one hand, and prescribers, purchasers and formulary managers, on the other. Although there are several statutory exceptions and regulatory safe harbors protecting certain common activities from prosecution, the exceptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor. In addition, the intent standard under the federal Anti-Kickback Statute was amended by the Affordable Care Act 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. Moreover, the government may assert 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 FCA.
- The federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), which prohibits, among other things, knowingly and willfully executing, or attempting to execute, a scheme or artifice to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private), willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false, fictitious or fraudulent statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.
- Patient data privacy and security regulation, including, in the United States, HIPAA, as amended by the Health Information Technology for Clinical Health Act of 2009 ("HITECH"), and their respective implementing regulations, which impose specified requirements on "covered entities," including healthcare providers, health plans, and healthcare clearinghouses, as well as their respective "business associates" that perform services for them that involve the use, or disclosure of, individually identifiable health information relating to the privacy, security and transmission of individually identifiable health information.

- The federal transparency requirements under the Physician Payments Sunshine Act, enacted as part of the Affordable Care Act, that require applicable manufacturers of covered drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to track and annually report to CMS payments and other transfers of value provided to physicians, as defined by such law, and teaching hospitals and certain ownership and investment interests held by physicians or their immediate family members in the applicable manufacturer, and disclosure of such information will be made by CMS on a publicly available website.
- Analogous state, local or foreign laws, such as state anti-kickback and false claims laws, which may apply to items or services reimbursed by any third-party payor, including commercial insurers; state and local marketing and/or transparency laws applicable to manufacturers that may be broader in scope than the federal requirements; state laws that require biopharmaceutical companies to comply with the biopharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government; state and local laws that require licensure or registration by sales and marketing agents of a pharmaceutical company; state laws that require disclosure of information related to drug pricing; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect as HIPAA.

Pharmaceutical and other healthcare companies have been prosecuted under these laws for a variety of promotional and marketing activities, such as: providing free trips, free goods, sham consulting fees and grants and other monetary benefits to prescribers; reporting to pricing services inflated average wholesale prices that were then used by federal programs to set reimbursement rates; engaging in off-label promotion; and submitting inflated best price information to the Medicaid Rebate Program to reduce liability for Medicaid rebates. Ensuring that our internal operations and future business arrangements with third parties comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations.

The global data protection landscape is rapidly evolving, and we may be affected by or subject to new, amended or existing laws and regulations in the future, including as our operations continue to expand or if we operate in foreign jurisdictions. For example, in June 2018, California enacted the California Consumer Privacy Act of 2018 (the "CCPA"), which took effect on January 1, 2020. The CCPA gives California residents the right to access and require deletion of their personal information, the right to opt out of certain personal information sharing, and the right to detailed information about how their personal information is collected, used and shared. The CCPA provides civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. Although the CCPA includes exemptions for certain clinical trials data, the law may increase our compliance costs and potential liability with respect to other personal information we collect about California residents. The CCPA has prompted a wave of proposals for new federal and state privacy legislation that, if passed, could increase our potential liability, increase our compliance costs and adversely affect our business. Several foreign jurisdictions, including the European Union (EU), its member states, the United Kingdom, Japan and Australia, among others, have adopted legislation and regulations that increase or change the requirements governing the collection, use, disclosure and transfer of the personal information of individuals in these jurisdictions. Additionally, certain countries have passed or are considering passing laws that require local data residency and/or restrict the international transfer of data. These laws have the potential to increase costs of compliance, risks of noncompliance and penalties for noncompliance.

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, disgorgement, fines, imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, additional oversight and reporting obligations, contractual damages, reputational harm, diminished profits and future earnings, 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 significant criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

We depend on our information technology systems and those of our third-party collaborators, service providers, contractors or consultants. Our internal computer systems, or those of our third-party collaborators, service providers, contractors or consultants, may fail or suffer security breaches, disruptions, or incidents, which could result in a material disruption of our development programs or loss of data or compromise the privacy, security, integrity or confidentiality of sensitive information related to our business and have a material adverse effect on our reputation, business, financial condition or results of operations.

In the ordinary course of our business, we collect, store and transmit large amounts of confidential information, including intellectual property, proprietary business information and personal information. Our internal technology systems and infrastructure, and those of our current or future third-party collaborators, service providers, contractors and consultants are vulnerable to damage from computer viruses, unauthorized access or use resulting from malware, natural disasters, terrorism, war and telecommunication and electrical failures, denial-of-service attacks, cyber-attacks or cyber-intrusions over the Internet, hacking, phishing and other social engineering attacks, persons inside our organizations (including employees or contractors), loss or theft, or persons with access to systems inside our organization. Attacks on information technology systems are increasing in their frequency, levels of persistence, sophistication and intensity, and they are being conducted by increasingly sophisticated and organized foreign governments, groups and individuals with a wide range of motives and expertise. In addition to extracting or accessing sensitive information, such attacks could include the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering and other means to affect service reliability and threaten the security, confidentiality, integrity and availability of information. The prevalent use of mobile devices that access sensitive information also increases the risk of data security incidents which could lead to the loss of confidential information or other intellectual property. While to our knowledge we have not experienced any material system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations or the operations of third-party collaborators, service providers, contractors and consultants, it could result in a material disruption of our development programs and significant reputational, financial, legal, regulatory, business or operational harm. The costs to us to mitigate, investigate and respond to potential security incidents, breaches, disruptions, network security problems, bugs, viruses, worms, malicious software programs and security vulnerabilities could be significant, and while we have implemented security measures to protect our data security and information technology systems, our efforts to address these problems may not be successful, and these problems could result in unexpected interruptions, delays, cessation of service and other harm to our business and our competitive position.

For example, the loss of clinical trial data from completed, ongoing or planned clinical trials for our product candidates could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any real or perceived security breach affects our systems (or those of our third-party collaborators, service providers, contractors or consultants), or results in the loss of or accidental, unlawful or unauthorized access to, use of, release of, or other processing of personally identifiable information or damage to our data or applications or other data or applications relating to our technology or product candidates, or inappropriate disclosure of confidential or proprietary information, we could incur liabilities and the further development of our product candidates could be delayed. Such a breach may require notification to governmental agencies, the media or individuals pursuant to various foreign, domestic (federal and state) privacy and security laws, if applicable, including HIPAA, as amended by HITECH, and its implementing rules and regulations, as well as regulations promulgated by the Federal Trade Commission and state breach notification laws. In addition, our liability insurance may not be sufficient in type or amount to cover us against claims related to security breaches, cyberattacks and other related incidents.

Any failure or perceived failure by us or any third-party collaborators, service providers, contractors or consultants to comply with our privacy, confidentiality, data security or similar obligations, or any data security incidents or other security breaches that result in the accidental, unlawful or unauthorized access to, use of, release of, processing of, or transfer of sensitive information, including personally identifiable information, may result in negative publicity, harm to our reputation, governmental investigations, enforcement actions, regulatory fines, litigation or public statements against us, could cause third parties to lose trust in us or could result in claims by third parties, including those that assert that we have breached our privacy, confidentiality, data security or similar obligations, any of which could have a material adverse effect on our reputation, business, financial condition or results of operations. To the extent we maintain individually identifiable health information, we could be subject to fines and penalties (including civil and criminal) under HIPAA for any failure by us or our business associates to comply with HIPAA's requirements. Moreover, data security incidents and other security breaches can be difficult to detect, and any delay in identifying them may lead to increased harm. While we have implemented data security measures intended to protect our information, data, information technology systems, applications and infrastructure, there can be no assurance that such measures will successfully prevent service interruptions or data security incidents.

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 European Economic Area in connection with our business, including in connection with conducting clinical trials in the European Economic Area (the "EEA"). Additionally, if any of our product candidates are approved, we may seek to commercialize those products in the European Economic Area. The collection and use of personal health data in the European Economic Area is governed by the provisions of the General Data Protection Regulation ((EU) 2016/679) (the "GDPR"), along with other European Union and country-specific laws and regulations. The United Kingdom and Switzerland have also adopted data protection laws and regulations. These legislative acts (together with regulations and guidelines) impose requirements relating to having legal bases for processing personal data relating to identifiable individuals and transferring such data outside of the European Economic Area, including to the United States, providing details to those individuals regarding the processing of their personal data, keeping personal data secure, having data processing agreements with third parties who process personal data, responding to individuals' requests to exercise their rights in respect of their personal data, reporting security breaches involving personal data to the competent national data protection authority and affected individuals, appointing data protection officers or corporate representatives, 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 European Economic Area and other states in the European Economic Area 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. European data protection authorities may interpret the GDPR and national laws differently and may impose additional requirements, which adds to the complexity of processing personal data in or from the EEA or United Kingdom. Guidance on implementation and compliance practices are often updated or otherwise revised.

Our insurance policies are expensive and only protect us from some business risks, leaving us exposed to significant uninsured liabilities.

We do not carry insurance for all categories of risk that our business may encounter. We believe that we maintain insurance customary for businesses of our size and type, including clinical trial liability insurance.

However, there are types of losses we may incur that cannot be insured against or that we believe are not economically reasonable to insure. Moreover, any loss incurred could exceed policy limits and policy payments made to us may not be made on a timely basis. Such losses could adversely affect our business prospects, results of operations, cash flows and financial condition. We do not know if our current levels of coverage are adequate or if we will be able to obtain insurance with adequate levels of coverage in the future, if at all. Any significant uninsured liability may require us to pay substantial amounts, which could materially and adversely affect our financial position and results of operations.

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, formulation supplier, manufacturing, clinical research organization 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.

If the market opportunities for any product that we or our strategic collaborators develop are smaller than we believe they are, our revenue may be adversely affected and our business may suffer.

We intend to initially focus our product candidate development on therapies for the treatment of liver and cardio-metabolic diseases. Our projections of addressable patient populations that have the potential to benefit from treatment with our product candidates are based on estimates. These estimates have been derived from a variety of sources, including the scientific literature, surveys of clinics, patient foundations or market research, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower than expected. Additionally, the potentially addressable patient population for our product candidates may not ultimately be amenable to treatment with our product candidates. Our market opportunity may also be limited by future competitor treatments that enter the market. If any of our estimates are inaccurate, the market opportunities for any of our product candidates could be significantly diminished and have an adverse material impact on our business.

Monitoring safety of patients receiving our product candidates is challenging, which could adversely affect our ability to obtain regulatory approval and commercialize.

For our ongoing clinical trial and planned clinical trials, we have and expect to contract with CROs and clinical trial sites experienced in the assessment and management of toxicities arising during clinical trials.

Nonetheless, these CROs and clinical trial sites may have difficulty observing patients and treating toxicities, which may be more challenging due to personnel changes, inexperience, shift changes, house staff coverage or related issues. This could lead to more severe or prolonged toxicities or even patient deaths, which could result in us or the FDA delaying, suspending or terminating one or more of our clinical trials, and which could jeopardize regulatory approval. We also expect the centers using our product candidates, if approved, on a commercial basis could similarly have difficulty in managing adverse events. Medicines used at centers to help manage adverse side effects of our product candidates may not adequately control the side effects and/or may have a detrimental impact on the efficacy of the treatment. Use of these medicines may increase with new physicians and centers administering our product candidates.

Unstable market and economic conditions may have serious adverse consequences on our business and financial condition.

Global credit and financial markets have experienced extreme disruptions at various points over the last few decades, characterized by diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. If another such disruption in credit and financial markets and deterioration of confidence in economic conditions occurs, our business may be adversely affected. If the equity and credit markets were to deteriorate significantly in the future, it may make any necessary debt or equity financing more difficult to complete, more costly, and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and share price and could require us to delay or abandon development or commercialization plans. In addition, there is a risk that one or more of our service providers, manufacturers or other partners would not survive or be able to meet their commitments to us under such circumstances, which could directly affect our ability to attain our operating goals on schedule and on budget.

We are subject to U.S. and certain foreign export and import controls, sanctions, embargoes, anti-corruption laws, and anti-money laundering laws and regulations. Compliance with these legal standards could impair our ability to compete in domestic and international markets. We can face criminal liability and other serious consequences for violations, which can harm our business.

We are subject to export control and import laws and regulations, including the U.S. Export Administration Regulations, U.S. Customs regulations, various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls, the U.S. Foreign Corrupt Practices Act of 1977, as amended, the U.S. domestic bribery statute contained in 18 U.S.C. § 201, the U.S. Travel Act, the USA PATRIOT Act, and other state and national anti-bribery and anti-money laundering laws in the countries in which we conduct activities. Anti-corruption laws are interpreted broadly and prohibit companies and their employees, agents, contractors, and other collaborators from authorizing, promising, offering, or providing, directly or indirectly, improper payments or anything else of value to recipients in the public or private sector. We may engage third parties to sell our products sell our products outside the United States, to conduct clinical trials, and/or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. We can be held liable for the corrupt or other illegal activities of our employees, agents, contractors, and other collaborators, even if we do not explicitly authorize or have actual knowledge of such activities. Any violations of the laws and regulations described above may result in substantial civil and criminal fines and penalties, imprisonment, the loss of export or import privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences.

Changes in our effective income tax rate could adversely affect our results of operations.

As an international company, we are subject to taxation in numerous countries, states and other jurisdictions. Our effective tax rate is derived from a combination of statutory tax rates in the various jurisdictions in which we operate. In preparing our financial statements, our effective tax rate is based on estimates of the amount of tax that will become payable in each of these jurisdictions. Our effective tax rate may, however, differ from estimates due to numerous factors, including a change in the mix of our profitability from country to country and changes in tax laws. The fluctuations in our effective tax rate could have an adverse effect on our business, financial condition and results of operations and cash flows.

Risks Related to Regulatory Approvals

BIO89-100 has not received regulatory approval. If we are unable to obtain regulatory approvals to market BIO89-100 or any future product candidates, our business will be adversely affected.

We do not expect BIO89-100 or any future product candidate to be commercially available for several years, if at all. BIO89-100 is and any future product candidate will be 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 BIO89-100 or any future product candidate. 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. The regulatory authorities in the United States and the EU have not approved any products for the treatment of NASH, and while there are recent guidelines issued by the FDA for the development of drugs for the treatment of NASH and a FDA surrogate endpoint table for drug approval that includes SHTG, it is unclear whether the requirements for approval will change in the future. Any such changes may require us to conduct new trials that could delay our timeframe and increase the costs of our programs related to BIO89-100 or any future product candidate for the treatment of NASH or SHTG. While the FDA has approved reduction in triglycerides levels as a surrogate endpoint for the full approval of drugs for the treatment of SHTG, it is unclear whether this endpoint will apply to any product candidates that we develop. If such endpoint is not deemed to apply to our product candidates, it would delay our development timeline and increase the costs of our programs for the treatment of SHTG. We have not had any discussions with the FDA regarding a surrogate endpoint or accelerated approval regulations. However, we currently expect that our SHTG program would be subject to smaller clinical trials and that we may expect a relatively quick overall development timeline for this indication. These expectations are based on a published FDA surrogate endpoint table for drug approval that includes SHTG, as well as the development path followed by other companies that developed an SHTG therapy.

However, we do not have a Special Protocol Assessment or other agreement with the FDA on the required clinical trials needed to support an application for approval of BIO89-100 in SHTG, and the overall clinical requirements and development timeline may be greater than expected. 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.

Even if we are able to obtain regulatory approvals for BIO89-100 or any future product candidate, 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 BIO89-100 or any future 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. We have not had any discussions with the FDA regarding a surrogate endpoint or accelerated approval regulations. However, based on recent guidelines issued by the FDA for the development of drugs for the treatment of NASH, if BIO89-100 is approved by the FDA based on a surrogate endpoint pursuant to section 506(c) of the Federal Food, Drug, and Cosmetic Act and the accelerated approval regulations (21 C.F.R. part 314, subpart H; 21 C.F.R. part 601, subpart E), consistent with FDA guidance, we will be required to conduct additional clinical trials establishing clinical benefit on the ultimate outcome of NASH. If BIO89-100 is approved by the FDA for the treatment of SHTG based on an endpoint of the reduction of triglycerides, the FDA may still require a cardiovascular outcomes study as part of a post-marketing authorization commitment. Such a study would be time consuming and costly and we cannot guarantee that we will see positive results, which could result in the revocation of the approval. 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 BIO89-100 and any future 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 revoked. As a result, we may 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.

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 BIO89-100 or any future product candidates would substantially harm our business.

Currently, we do not have any product candidates that have 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 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 BIO89-100 or any future product candidates will ever obtain regulatory approval.

BIO89-100 or any future product candidate could fail to receive regulatory approval from the FDA or comparable foreign regulatory authorities 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 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 a product candidate 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 comparable foreign regulatory authorities 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.

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

If we succeed in developing any products, we intend to market them in 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. 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. 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.

Even if BIO89-100 or any future product candidate receives regulatory approval, it 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, it may require labeling changes or establishment of a risk evaluation and mitigation strategy 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 studies;
- 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 product revenue.

Advertising and promotion of any product candidate that obtains approval in the United States will be heavily scrutinized by the FDA, the Department of Justice, the Department of Health and Human Services' 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 significant civil and criminal sanctions by the government. 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 significant civil and criminal penalties. Additionally, comparable foreign regulatory authorities will heavily scrutinize advertising and promotion of any product candidate that obtains approval outside of the United States.

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.

Risks Relating to 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 current or future licensors', licensees' or collaborators' ability to establish and maintain adequate protection of our owned and licensed 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 hold issued patents, we have applied for patents, and we 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 and other technologies relating to our programs. There can be no assurance that any of these patent applications will issue as patents or, for those applications that do mature into patents, that the claims of the patents will exclude others from making, using or selling our product candidates or products that compete with or are similar to our product candidates. In countries where we have not sought 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.

With respect to patent rights, we do not know whether any of the pending patent applications for any of our product candidates will result in the issuance of patents that effectively protect our technologies, processes and product candidates, or if any of our issued patents or our current or future licensors', licensees' or collaborators' issued patents will effectively prevent others from commercializing competitive technologies, processes and products. 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 BIO89-100 or any future product candidates 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 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 BIO89-100 or any future product candidates.

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 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 the patent rights of other biotechnology companies, the scope, validity and enforceability of our owned and licensed patent rights generally are highly uncertain and involve 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 those 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. We expect to seek extensions of patent terms for our issued patents, where available. This includes in the United States 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 comparable foreign regulatory authorities, 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 protective 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 may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use 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 have patent protection, but enforcement is not as strong as that in the United States. These products may compete with BIO89-100 or any future product candidates and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

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

The requirements for patentability differ and certain countries have heightened requirements for patentability, requiring more disclosure in the patent application. In addition, certain countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In those countries, we may have limited remedies if patents are infringed or if we 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 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.

We rely on a license from Teva and a sublicense from ratiopharm to patents and know-how related to glycoPEGylation technology that are used in the development, manufacture and commercialization of BIO89-100. Any termination or loss of significant rights, including the right to glycoPEGylation technology, or breach, under these agreements or any future license agreement related to our product candidates, would materially and adversely affect our ability to continue the development and commercialization of the related product candidates.

In April 2018, we entered into an Asset Transfer and License Agreement (the "FGF21 Agreement") with Teva under which we acquired certain patents, intellectual property and other assets relating to Teva's glycoPEGylated FGF21 program, including BIO89-100. Under this agreement, we were granted a perpetual, non-exclusive (but exclusive as to BIO89-100), non-transferable, worldwide license to patents and know-how related to glycoPEGylation technology used in the development, manufacture and commercialization of BIO89-100 and products containing BIO89-100. The FGF21 Agreement also contains numerous covenants with which we must comply, including the utilization of commercially reasonable efforts to develop and ultimately commercialize BIO89-100, as well as certain reporting covenants and the obligation to make royalty payments, if and when BIO89-100 is approved for commercialization. Our failure to satisfy any of these covenants could result in the termination of the FGF21 Agreement. In addition, we entered into a Sublicense Agreement with ratiopharm (the "ratiopharm Sublicense"), under which we were granted a perpetual, exclusive, worldwide sublicense to patents and know-how related to glycoPEGylation technology used in the development, manufacture and commercialization of BIO89-100 and products containing BIO89-100. Termination of the FGF21 Agreement or the ratiopharm Sublicense will impact our rights under the intellectual property licensed to us by Teva and ratiopharm, respectively, including our license to glycoPEGylation technology, but will not affect our rights under the assets assigned to us.

Beyond this agreement, our commercial success will also depend upon our ability, and the ability of our licensors, to develop, manufacture, market and sell our product candidates and use our 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 product candidates. As a result, we may enter into additional license agreements 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.

Any of the foregoing could materially and 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.

Changes in patent law could diminish the value of patents in general, thereby impairing our ability to protect BIO89-100 and any future 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 in recent years has issued rulings either narrowing the scope of patent protection available in certain circumstances or 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 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 ability to obtain new patents or to enforce existing patents and patents we may obtain in the future.

Patent reform laws, such as the Leahy-Smith America Invents Act (the "Leahy-Smith Act"), as well as changes in how patent laws are interpreted, could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents. The Leahy-Smith Act made 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, and a change 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. The Leahy-Smith Act and its implementation may increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our 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 technology necessary to develop and commercialize BIO89-100 and any future product candidates.

The patent landscape around our programs is complex, and we are aware of several third-party patents and patent applications containing subject matter that might be relevant to BIO89-100. Depending on what claims ultimately issue from these patent applications, and how courts construe the issued patent claims, as well as depending on the ultimate formulation and method of use of BIO89-100 or any future 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 the relevant license agreements, or such license agreements are terminated for any other reasons, we may lose our rights to the technologies licensed under those agreements.

The licensing or acquisition of third-party intellectual property rights is an area in which many companies operate that have interests that are in conflict with ours, and several 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 patents or misappropriate or otherwise violate our intellectual property rights. In the future, we may initiate legal proceedings to enforce or defend our intellectual property rights, to protect our 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 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 patents, requiring us to engage in complex, lengthy and costly litigation or other proceedings. These proceedings can be expensive and time-consuming and many of our adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we can. Accordingly, despite our efforts, we 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 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, defendants usually assert counterclaims alleging invalidity or unenforceability. 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 subject matter alleged to be infringing on the grounds that our patents do not cover that subject matter. An adverse result in any litigation proceeding could put one or more of our 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, or opposition, derivation, revocation, reexamination, *inter partes* review or interference proceedings, or other pre-issuance or post-grant proceedings or other patent office proceedings or litigation in the United States or other jurisdictions provoked by third parties or brought by us, may be necessary to determine the inventorship, priority, patentability or validity of inventions with respect to our 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 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 in such a case does not offer us a license on commercially reasonable terms, or at all. Even if we obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In addition, if the breadth or strength of protection provided by our 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 our defense 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 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 our business.

Our commercial success depends upon our ability to develop, manufacture, market and sell BIO89-100 and any future 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 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, 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 adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we can.

We could be found liable for monetary damages, including treble damages and attorneys' fees, if we are found to have willfully infringed a patent of a third party. A finding of infringement could prevent us from commercializing our BIO89-100 or any future product candidates or force us to cease some of our business operations, which could materially harm our business.

We may not be aware of all third-party intellectual property rights potentially relating to BIO89-100 or any future product candidates and technologies. 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 cover our product candidates. 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 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 other commercialization partners and we were unable to successfully challenge the validity or enforceability of any such asserted patents, then we 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.

Although we have reviewed certain third-party patents and patent filings that we believe may be relevant to our therapeutic candidates or products, we have not conducted a freedom-to-operate search or analysis for any of our therapeutic candidates or products, and we may not be aware of patents or pending or future patent applications that, if issued, would block us from commercializing our therapeutic candidates or products. Thus, we cannot guarantee that our therapeutic candidates or products, or our commercialization thereof, do not and will not infringe any third party's intellectual property.

We may be subject to claims by third parties asserting misappropriation of intellectual property, or claiming ownership of what we regard as our own intellectual property.

Although we seek 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 the services of 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.

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 product candidates, we also rely substantially on trade secrets, 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 trade secrets and there may be no adequate remedy available for such breach of an agreement. We cannot assure you that our trade secrets 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 technology or information that we protect as trade secret, 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 BIO89-100 and any future product candidates we may develop or utilize similar technology but that are not covered by the claims of the patents that we exclusively license or may own in the future;
- we, or our future collaborators, might not have been the first to make the inventions covered by the issued patents and pending patent applications that we exclusively license or may own in the future;
- we, or our 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 exclusively licensed intellectual property rights;
- it is possible that our pending patent applications or those that we may file in the future will not result in issued patents;
- issued patents that we hold rights to 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 major commercial markets in which we do not have sufficient patent rights to stop such sales;
- we may not develop additional proprietary technologies that are patentable;
- the patents of others may be asserted against our product candidates and technologies in a manner that harms 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 trade secrets or know-how.

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

If our trademarks and trade names are not maintained and adequately protected, we may not be able to build name recognition in our markets of interest, and our business may be adversely affected.

Failure to obtain trademark registrations in the future, could limit our ability to protect and enforce our trademarks and impede our marketing efforts in the countries in which we operate. We may not be able to protect our rights to trademarks and trade names which we may need to build name recognition with potential partners or customers in our markets of interest. As a means to enforce any future trademark rights and prevent infringement, we may be required to file trademark claims against third parties or initiate trademark opposition proceedings. This can be expensive, and strain the financial resources of a company of our size, and time-consuming, and we may not be successful in enforcing our trademark rights. In addition, our registered or unregistered trademarks or trade names may be challenged, infringed, circumvented, declared generic or determined to be infringing on other marks.

Future trademark applications in the United States and in other foreign jurisdictions where we may file may not be allowed or may subsequently be opposed. Even if these applications result in registration of trademarks, third parties may challenge our use or registration of these trademarks in the future. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected.

Risks Related to Ownership of Our Common Stock

The price of our common stock may be volatile, and you may lose all or part of your investment.

The market price of our common stock could fluctuate significantly, and you may not be able to resell your shares at or above the price you paid for your shares. Those fluctuations could be based on various factors in addition to those otherwise described in this prospectus, including those described in these "Risk Factors." Any of these factors may result in large and sudden changes in the volume and trading price of our common stock. In the past, following periods of volatility in the market price of a company's securities, stockholders have often instituted securities class action litigation against that company. If we were involved in a class action suit, it could divert the attention of management, result in negative press reports and, if adversely determined, have a material adverse effect on our results of operations and financial condition.

In addition, the stock market, in general, and the stocks of many small healthcare 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. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. Further, a decline in the broader financial markets and related factors beyond our control may cause the price of our common stock to decline rapidly and unexpectedly.

Sales of our common stock, or the perception that such sales may occur, could depress the price of our common stock.

Sales of a substantial number of shares of our common stock in the public market, or the perception that such sales may occur, could depress the market price of our common stock. Holders of an aggregate of 7,077,366 shares 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. In addition, we have filed a registration statement registering under the Securities Act the shares of our common stock reserved for issuance under our 2019 Equity Incentive Plan, including shares issuable upon exercise of outstanding options. These shares can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates and the lock-up agreements described above. Further, as opportunities present themselves, we may enter into financing or similar arrangements in the future, including the issuance of debt or equity securities. If we issue common stock or securities convertible into our common stock, our common stockholders would experience additional dilution and, as a result, the price of our common stock may decline.

Our directors, executive officers and current holders of 5% or more of our capital stock have substantial control over our company, which could limit your ability to influence the outcome of matters subject to stockholder approval, including a change of control.

As of March 1, 2020, our executive officers, directors and other holders of 5% or more of our common stock beneficially owned a majority of our outstanding common stock. As a result, our executive officers, directors and other holders of 5% or more of our common stock, if they act, will be able to influence or control matters requiring approval by our stockholders, including the election of directors and the approval of mergers, acquisitions or other extraordinary transactions. In addition, our current directors, executive officers and other holders of 5% or more of our common stock, acting together, would have the ability to control the management and affairs of our company. They may also have interests that differ from yours and may vote in a way with which you disagree and that may be adverse to your interests. This concentration of ownership may have the effect of delaying, preventing or deterring a change of control of our company, could deprive our stockholders of an opportunity to receive a premium for their shares of our common stock as part of a sale of our company and could affect the market price of our common stock.

If securities or industry analysts do not publish research, or publish inaccurate or unfavorable research, about our stock or business, the price of our common stock 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. If one or more of the analysts who cover us downgrade our stock or publish inaccurate or unfavorable research about our business, demand for our common stock could decrease and the price of our common stock could decline. In addition, if our operating results fail to meet the forecast of analysts, the price of our common stock would likely decline. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, demand for our stock could decrease, which might cause the price of our common stock and trading volume to decline.

We have identified material weaknesses in our internal control over financial reporting. If our remediation of the material weaknesses is not effective, or if we experience additional material weaknesses or otherwise fail to maintain an effective system of internal controls in the future, we may not be able to produce timely and accurate financial statements, and we or our independent registered public accounting firm may conclude that our internal control over financial reporting is not effective, which could adversely affect our investors' confidence and our stock price.

Prior to our initial public offering, we were a private company and were not required to test our internal controls on a systematic basis. As an emerging growth company under the JOBS Act, our management will be required to report upon the effectiveness of our internal control over financial reporting under Section 404 ("Section 404") of the Sarbanes-Oxley Act of 2002, as amended (the "Sarbanes-Oxley Act") beginning with our Annual Report on Form 10-K for the year ending December 31, 2020. Our independent registered public accounting firm is not required to formally attest to the effectiveness of our internal control over financial reporting until the date we are no longer an emerging growth company and reach accelerated filer status.

Effective internal controls over financial reporting are necessary for us to provide reliable financial information and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation, could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our consolidated financial statements or identify other areas for further attention or improvement. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual or interim consolidated financial statements will not be prevented or detected on a timely basis.

In connection with our financial statement close process for 2018, we identified material weaknesses in the design and operating effectiveness of our internal control over financial reporting.

These material weaknesses related to the following:

- We did not have an internal finance department. Consequently, we lacked sufficient personnel with an appropriate level of knowledge and requisite U.S. generally accepted accounting principles expertise to identify, evaluate and account for complex and non-routine transaction and an adequate supervisory review structure that is needed to comply with financial reporting requirements.
- We did not have an adequate assessment of risks that could significantly impact internal control over financial reporting and did not effectively design and monitor controls in response to the risks of material misstatement.

We have implemented and are in the process of implementing measures designed to improve our disclosure controls and procedures and internal control over financial reporting to address the underlying causes of these material weaknesses, including the implementation of appropriate segregation of duties, formalization of accounting policies and controls, implementation of accounting systems to automate manual processes, formalization of our hiring practices, hiring of our Chief Financial Officer, principal accounting officer and additional qualified accounting and finance personnel, recruitment of a new audit committee chair and financial expert (following the resignation of Tomer Kariv, our audit committee chair and financial expert, from our board of directors in December 2019) and engagement of financial consultants to enable the implementation of internal controls over financial reporting.

Our remediation efforts are ongoing. While we believe that these efforts have improved and will continue to improve our internal control over financial reporting, remediation of the material weaknesses will require validation and testing of the design and operating effectiveness of internal controls over a sustained period of financial reporting cycles. We cannot assure you that these measures will significantly improve or remediate the material weaknesses described above. We, and our independent registered public accounting firm, were not required to perform an evaluation of our internal control over financial reporting as of December 31, 2019 in accordance with the provisions of the Sarbanes-Oxley Act. Accordingly, we cannot assure you that we have identified all material weaknesses or that there will not be additional material weaknesses or deficiencies that we will identify.

We are required to comply with Section 404, which requires management to certify financial and other information in our quarterly and annual reports and provide an annual management report on the effectiveness of our internal control over financial reporting commencing with our second annual report. To achieve compliance with Section 404 we will need to continue to dedicate internal resources, outside consultants and continue to execute a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes, as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404 and material weaknesses may still exist. We also cannot assure you that there will not be additional material weaknesses or significant deficiencies in our internal controls in the future. In the event that we are not able to successfully remediate the existing material weaknesses in our internal control over financial reporting or 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 consolidated financial statements, investors may lose confidence in our operating results, our stock price could decline and we may not be able to remain listed on The Nasdaq Global Market.

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

As a public company, we have and will continue to incur significant legal, accounting 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, the Dodd-Frank Wall Street Reform and Protection Act, as well as rules adopted, and to be adopted, by the SEC and Nasdaq. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, we expect these rules and regulations to substantially increase our legal and financial compliance costs and to make some activities more time-consuming and costly.

The increased costs will increase our net loss. For example, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be forced to accept reduced policy limits or incur substantially higher costs to maintain the same or similar 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.

We are an emerging growth company, as defined in the Securities Act, and we cannot be certain if the reduced disclosure requirements applicable to emerging growth companies will make our common stock less attractive to investors.

We are an emerging growth company, as defined in Section 2(a) of the Securities Act, as modified by the JOBS Act, and we may take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including relief from the auditor attestation requirements of Section 404 less extensive disclosure obligations regarding executive compensation in our registration statements, periodic reports and proxy statements, exemptions from the requirements to hold a nonbinding advisory vote on executive compensation, and exemptions from stockholder approval of any golden parachute payments not previously approved. As a result, our stockholders may not have access to certain information that they may deem important. We could be an emerging growth company for up to five years, although circumstances could cause us to lose that status earlier.

In addition, the JOBS Act also provides that an emerging growth company can take advantage of the extended transition period provided in the Securities Act for complying with new or revised accounting standards. An emerging growth company can therefore delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to avail ourselves of this exemption and, as a result, will not be subject to the same implementation timing for new or revised accounting standards as for other public companies that are not emerging growth companies, which may make comparison of our consolidated financial statements to those of other public companies more difficult.

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 the price of our common stock may be more volatile.

Because we do not expect to pay dividends in the foreseeable future, you must rely on price appreciation of our common stock for return on your investment.

We intend to retain most, if not all, of our available funds and earnings to fund the development and growth of our business. As a result, we do not expect to pay any cash dividends in the foreseeable future.

Therefore, you should not rely on an investment in our common stock as a source for any future dividend income.

Our board of directors has significant discretion as to whether to distribute dividends and in what amounts. Even if our board of directors decides to declare and pay dividends, the timing, amount and form of future dividends, if any, will depend on, among other matters, our future results of operations and cash flow, our capital requirements and surplus, the amount of distributions, if any, received by us from our subsidiaries, our financial condition, contractual restrictions and other factors deemed relevant by our board of directors.

Our amended and restated certificate of incorporation, amended and restated bylaws and Delaware law could prevent a third party from acquiring us (even if an acquisition would benefit our stockholders), may limit the ability of our stockholders to replace our management and limit the price that investors might be willing to pay for shares of our common stock.

Our amended and restated certificate of incorporation and our amended and restated bylaws could have the effect of making it more difficult for a third party to acquire, or of discouraging a third party from attempting to acquire, control of us. These provisions could delay or prevent a change in control of the company and could limit the price that investors might be willing to pay in the future for shares of our common stock. These provisions, among other things.

- establish a staggered 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;
- authorize our board of directors to issue new series of preferred stock without stockholder approval and create, subject to applicable law, a series of preferred stock with preferential rights to dividends or our assets upon liquidation, or with superior voting rights to our existing common stock;
- eliminate the ability of our stockholders to call special meetings of stockholders;
- eliminate the ability of our stockholders to fill vacancies on our board of directors;
- establish advance notice requirements for nominations for election to our board of directors or for proposing matters that can be acted upon by stockholders at our annual stockholder meetings;
- permit our board of directors to establish the number of directors;
- provide that our board of directors is expressly authorized to make, alter or repeal our amended and restated bylaws;
- provide that shareholders can remove directors only for cause and only upon the approval of not less than 66$^{2/3}$ of all outstanding shares of our voting stock;
- require the approval of not less than 66$^{2/3}$ of all outstanding shares of our voting stock to amend our bylaws and specific provisions of our certificate of incorporation; and
- limit the jurisdictions in which certain stockholder litigation may be brought.

As a Delaware corporation, we are subject to the anti-takeover provisions of Section 203 of the Delaware General Corporation Law, which prohibits a Delaware corporation from engaging in a business combination specified in the statute with an interested stockholder (as defined in the statute) for a period of three years after the date of the transaction in which the person first becomes an interested stockholder, unless the business combination is approved in advance by a majority of the independent directors or by the holders of at least two-thirds of the outstanding disinterested shares. The application of Section 203 of the Delaware General Corporation Law could also have the effect of delaying or preventing a change of control of us.

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 Delaware General Corporation Law, 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 Delaware 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 the 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, under the Securities Act, federal courts have concurrent jurisdiction over all suits brought to enforce any duty or liability created by the Securities Act, and investors cannot waive compliance with the federal securities laws and the rules and regulations thereunder, and the Court of Chancery of the State of Delaware recently 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 may be reviewed and ultimately overturned by the Delaware Supreme Court. If the Court of Chancery's decision were to be overturned, we would enforce the federal district court exclusive forum provision in our amended and restated certificate of incorporation.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

We lease office space, which consists of approximately 1,600 square feet located at 6 Hamada Street, Herzliya, 4673340, Israel. This lease expires on April 30, 2020. We also lease office space at 142 Sansome Street, San Francisco, California 94104, which consists of approximately 3,600 square feet. This lease expires on January 14, 2022. We believe that our current spaces are adequate for our needs. We also believe we will be able to obtain additional space, as needed, on commercially reasonable terms.

Item 3. Legal Proceedings.

We are currently not a party to any material legal proceedings. From time to time, we may become involved in legal proceedings arising in the ordinary course of our business. Regardless of outcome, litigation can have an adverse impact on us due to defense and settlement costs, diversion of management resources, negative publicity, reputational harm and other factors, and there can be no assurances that favorable outcomes will be obtained.

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 is traded on The Nasdaq Global Market under the symbol "ETNB."

As of March 1, 2020, there were approximately 11 stockholders of record of our common stock.

Dividend Policy

We have never declared or paid cash dividends on our capital stock and have no present intention to pay cash dividends on our common stock for the foreseeable future. Any determination to pay dividends to holders of our common stock will be at the discretion of our board of directors and will depend on many factors, including our financial condition, results of operations, liquidity, earnings, projected capital and other cash requirements, legal requirements, restrictions in the agreements governing any indebtedness we may enter into, business prospects and other factors that our board of directors deems relevant.

Use of Proceeds from our Initial Public Offering

On November 13, 2019, we completed our IPO, pursuant to which we issued and sold an aggregate of 6,100,390 shares of common stock (inclusive of 795,703 shares pursuant to the underwriters' option to purchase additional shares) at the IPO price of $16.00 per share. The aggregate gross proceeds from our IPO were $97.6 million, and the net proceeds were $87.7 million after deducting underwriting discounts and commissions of $6.8 million and other offering expenses of $3.1 million. The offer and sale of the shares of common stock in the IPO were registered pursuant to registration statements on Form S-1 (File Nos. 333-234174 and 333-234617), which the SEC declared effective on November 8, 2019. No offering expenses were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning 10% or more of any class of our equity securities or to any other affiliates. The underwriters for our IPO were BofA Securities, Inc., SVB Leerink LLC, RBC Capital Markets, LLC, and Oppenheimer & Co. Inc.

There has been no material change in the intended use of proceeds from our IPO as described in our final prospectus filed with the SEC pursuant to Rule 424(b)(4) on November 12, 2019.

Item 6. Selected Financial Data.

We are a smaller reporting company, as defined by Rule 12b-2 under the Securities and Exchange Act of 1934 and in Item 10(f)(1) of Regulation S-K, and are not required to provide the information under this item.

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

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and related notes and other financial information included elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis includes forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those described in or implied by these forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those identified below and those discussed in the section titled "Risk Factors" included elsewhere in this Annual Report on Form 10-K.

Overview

We are a clinical-stage biopharmaceutical company focused on the development and commercialization of innovative therapies for the treatment of liver and cardio-metabolic diseases. Our lead product candidate, BIO89-100, a specifically engineered glycoPEGylated analog of FGF21, is currently being developed for the treatment of NASH. NASH is a severe form of NAFLD, characterized by inflammation and fibrosis in the liver that can progress to cirrhosis, liver failure, HCC and death. There are currently no approved products for the treatment of NASH. FGF21 is a clinically-validated mechanism that has been shown in humans to reduce steatosis and address cardio-metabolic dysregulation. We believe BIO89-100 may be a differentiated FGF21 therapy based on its robust and durable biological effects and a favorable tolerability profile, as well as its potential for a longer dosing interval. Combining these characteristics with the ability to address the key liver pathologies in NASH, as well as the underlying metabolic dysregulation in NASH patients, BIO89-100 has the potential to become a mainstay of NASH therapy. We successfully completed a Phase 1a, first-in-human, SAD clinical trial with 58 healthy volunteers. The magnitude and significance of BIO89-100's biological effects after a single dose on lipid parameters were robust and durable. In July 2019, we initiated our POC Phase 1b/2a clinical trial in patients with NASH or patients with NAFLD and a high risk of NASH and we expect to report topline data in the second half of 2020. We also intend to develop BIO89-100 for the treatment of SHTG, a condition identified by severely elevated levels of triglycerides (greater than or equal to 500 mg/dL), which is associated with an increased risk of NASH, cardiovascular events and acute pancreatitis. We expect to initiate our Phase 2 trial in SHTG patients in the first half of 2020 in order to evaluate the ability of BIO89-100 to reduce fasting plasma triglyceride levels compared to baseline levels and to report topline data in the first half of 2021. Based on FDA guidance for the development of SHTG treatments, as well as the regulatory path followed by other companies that have successfully developed SHTG therapies, we believe that a combination of smaller clinical trials and shorter development timelines could mean that SHTG potentially represents a quicker path to market for BIO89-100. We believe BIO89-100 has the potential to address multiple drivers underlying metabolic dysregulation, which would make it an ideal candidate for selected liver and cardio-metabolic diseases.

We commenced operations in 2018 and have devoted substantially all of our resources to organizing and staffing our company, business planning, raising capital, acquiring our initial product candidate, BIO89-100, and licensing certain related technology, conducting research and development activities, including preclinical studies and early clinical trials, and providing general and administrative support for these operations. We have funded our operations since our inception to December 31, 2019 through the issuance and sale of capital stock. As of December 31, 2019, our cash and cash equivalents totaled $93.3 million. Based on our current operating plan, we believe that our cash and cash equivalents will be sufficient to meet our anticipated cash requirements into the second half of 2021.

On November 8, 2019, our Registration Statements on Form S-1 (File No. 333-234174 and 333-234617) relating to our IPO, were declared effective by the SEC. Pursuant to the Registration Statements, we issued and sold an aggregate of 6,100,390 shares of common stock (inclusive of 795,703 shares pursuant to the underwriters' option to purchase additional shares) at a price of $16.00 per share for aggregate cash proceeds of $87.7 million, net of underwriting discounts and commissions and estimated offering costs. Both the sale and issuance of 5,304,687 shares in the IPO and the sale and issuance of an additional 795,703 shares pursuant to the underwriters' option to purchase additional shares closed on November 13, 2019. Upon the closing of the IPO, all outstanding shares of convertible preferred stock automatically converted into 7,077,366 shares of common stock. Subsequent to the closing of the IPO, there were no shares of preferred stock outstanding.

We have incurred net losses since our inception. Our net losses were $57.4 million and $16.2 million for 2019 and the period from January 18 (inception) to December 31, 2018, respectively. As of December 31, 2019, we had an accumulated deficit of $73.6 million. We expect to continue to incur significant expenses and increasing operating losses as we advance BIO89-100 and any future product candidates through clinical trials, seek regulatory approval for BIO89-100 and any future product candidates, expand our clinical, regulatory, quality, manufacturing and commercialization capabilities, protect our intellectual property, prepare for and, if approved, proceed to commercialization of BIO89-100 and any future product candidates, expand our general and administrative support functions, including hiring additional personnel, and incur additional costs associated with operating as a public company. Our net losses may fluctuate significantly from quarter-to-quarter and year-to-year, depending on the timing of our clinical trials and our expenditures on other research and development activities.

We have never generated revenue and do not expect to generate revenue from product sales unless and until we successfully complete development and obtain regulatory approval for BIO89-100, which we expect will not be for at least several years, if ever. Accordingly, until such time as we can generate significant revenue from sales of BIO89-100, if ever, we expect to finance our cash needs through a combination of public or private equity offerings, debt financings or other capital sources, including potential collaborations, licenses and other similar arrangements. However, we may be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. Our failure to raise capital or enter into such other arrangements when needed would have a negative impact on our financial condition and could force us to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Reorganization

We were incorporated in January 2018 in Israel under the name 89Bio Ltd. 89bio, Inc. was incorporated in June 2019 for the purpose of an internal reorganization transaction. In September 2019, all of the equity holders of 89Bio Ltd. exchanged 100% of the equity of 89Bio Ltd. for 100% of the equity of 89bio, Inc (the "Reorganization"). Following this reorganization, 89Bio Ltd. became a wholly owned subsidiary of 89bio, Inc. The Reorganization was retrospectively adjusted to inception given the transaction was between entities under common control.

Agreements with Teva

In April 2018, we entered into the FGF21 Agreement with Teva, under which we acquired certain patents, intellectual property and other assets relating to Teva's glycoPEGylated FGF21 program, including BIO89-100. Under the FGF21 Agreement, Teva also granted us a perpetual, non-exclusive (but exclusive as to BIO89-100), non-transferable, worldwide license to patents and know-how related to glycoPEGylation technology for use in the research, development, manufacture and commercialization of BIO89-100 and products containing BIO89-100. We also entered into an Asset Transfer and License Agreement with Teva under which we acquired from Teva certain patents, intellectual property and other assets relating to Teva's development program of small molecule inhibitors of FASN (the "FASN Agreement" and collectively with the FGF21 Agreement, the "Teva Agreements").

Pursuant to the Teva Agreements, we paid Teva a nonrefundable upfront payment of $6.0 million in 2018. In addition, we are required to make certain payments to Teva under each of the Teva Agreements of up to $2.5 million for the achievement of certain development milestones, and additional payments of up to $65.0 million upon achievement of certain commercial milestones, for a total under both Teva Agreements of up to $135.0 million. We are also obligated to pay Teva tiered royalties at percentages in the low-to-mid single-digits on worldwide net sales of products containing BIO89-100 or FASN.

The assets acquired from Teva did not meet the definition of a business and therefore, this acquisition was treated as an asset acquisition for accounting purposes. In addition, we recorded the total consideration transferred to Teva in connection with this acquisition as research and development expense because the acquired technology represented in-process research and development and had no alternative future use.

Components of Results of Operations

Research and Development Expenses

Research and development expenses consist primarily of costs incurred for the development of our lead product candidate, BIO89-100. Our research and development expenses consist primarily of external costs related to preclinical and clinical development, including costs related to acquiring patents and intellectual property, expenses incurred under license agreements and agreements with contract research organizations and consultants, costs related to acquiring and manufacturing clinical trial materials, including under agreements with contract manufacturing organizations and other vendors, costs related to the preparation of regulatory submissions and expenses related to laboratory supplies and services, as well as personnel costs. Personnel costs consist of salaries, employee benefits and share-based compensation for individuals involved in research and development efforts.

We expense all research and development expenses in the periods in which they are incurred. We accrue for costs incurred as the services are being provided by monitoring the status of specific activities and the invoices received from our external service providers. We adjust our accrual as actual costs become known.

Payments associated with licensing agreements to acquire licenses to develop, use, manufacture and commercialize products that have not reached technological feasibility and do not have alternate commercial use are expensed as incurred. Where contingent milestone payments are due to third parties under research and development arrangements or license agreements, the milestone payment obligations are expensed when the milestone results are probable and estimable, which is generally upon achievement of milestones.

We expect our research and development expenses to increase substantially for the foreseeable future as we continue the development of BIO89-100 and continue to invest in research and development activities. The process of conducting the necessary clinical research to obtain regulatory approval is costly and time consuming, and the successful development of BIO89-100 and any future product candidates is highly uncertain. To the extent that BIO89-100 continues to advance into larger and later stage clinical trials, our expenses will increase substantially and may become more variable. The actual probability of success for BIO89-100 or any future product candidate may be affected by a variety of factors, including the safety and efficacy of our product candidates, investment in our clinical programs, manufacturing capability and competition with other products. As a result, we are unable to determine the timing of initiation, duration and completion costs of our research and development efforts or when and to what extent we will generate revenue from the commercialization and sale of BIO89-100 or any future product candidate.

Our future clinical development costs may vary significantly based on factors such as:

- the cost and timing of manufacturing BIO89-100 and any future product candidates;
- per-patient trial costs;
- the number of trials required for approval;
- the number of sites included in the trials;
- the countries in which the trials are conducted;
- the length of time required to enroll eligible patients;
- the number of patients that participate in the trials;
- the number of doses evaluated in the trials;
- the drop-out or discontinuation rates of patients;
- potential additional safety monitoring requested by regulatory agencies;
- the duration of patient participation in the trials and follow-up;
- the phase of development of BIO89-100 and any future product candidates; and
- the efficacy and safety profile of BIO89-100 and any future product candidates.

General and Administrative Expenses

Our general and administrative expenses consist primarily of personnel costs, expenses for outside professional services, including legal, human resource, audit and accounting services, consulting costs and allocated facilities costs. Personnel and related costs consist of salaries, benefits and share-based compensation for personnel in executive, finance and other administrative functions. Facilities costs consist of rent and maintenance of facilities. We expect our general and administrative expenses to increase for the foreseeable future as we increase the size of our administrative function to support the growth of our business and support our continued research and development activities. We also anticipate increased expenses as a result of operating as a public company, including increased expenses related to audit, legal, regulatory and tax-related services associated with maintaining compliance with exchange listing and SEC requirements, director and officer insurance premiums and investor relations costs.

Other Expenses (Income), Net

Other expenses (income), net primarily consists of the revaluation of our convertible preferred stock liability.

Results of Operations

Year Ended December 31, 2019 and the Period from January 18, 2018 (inception) to December 31, 2018

The following table summarizes our results of operations for the periods presented (in thousands):

	Year Ended December 31, 2019	Period from January 18, 2018 (inception) to December 31, 2018	Increase/ (Decrease)
Operating expenses:			
Research and development	$ 21,346	$ 13,681	$ 7,665
General and administrative	5,294	1,481	3,813
Total operating expenses	26,640	15,162	11,478
Loss from operations	26,640	15,162	11,478
Other expenses (income), net	30,562	986	29,576
Income tax expense	218	28	190
Net loss and comprehensive loss	$ 57,420	$ 16,176	$ 41,244

Research and Development Expenses

The following table summarizes the period-over-period changes in research and development expenses for the periods indicated (in thousands):

	Year Ended December 31, 2019	Period from January 18, 2018 (inception) to December 31, 2018	Increase/ (Decrease)
Up-front license payment to Teva	$ —	$ 6,000	$ (6,000)
Clinical development	5,453	1,826	3,627
Contract manufacturing	7,257	3,379	3,878
Pre-clinical costs	4,072	1,207	2,865
Personnel-related expenses	3,688	1,013	2,675
Other expenses	876	256	620
Total research and development expenses	$ 21,346	$ 13,681	$ 7,665

Research and development expenses increased by $7.7 million, or 56%, to $21.4 million for the year ended December 31, 2019 from $13.7 million during the period from January 18, 2018 (inception) to December 31, 2018. The increase was primarily due to an increase of $3.9 million in contract manufacturing costs, an increase of $3.6 million in clinical development costs as we continue to advance our current clinical programs with our lead product candidate, BIO89-100 and an increase of $2.9 million in pre-clinical costs. In addition, personnel-related costs, including share-based compensation, increased by $2.7 million and other expenses increased by $0.6 million due to increased headcount and other costs as we ramped up our operations. These increases were partially offset by a $6.0 million decrease due to an up-front license payment to Teva during the period from January 18, 2018 (inception) to December 31, 2018 and there were no such license payment expenses related to Teva during the year ended December 31, 2019.

General and Administrative Expenses

General and administrative expenses increased by $3.8 million, or 257%, to $5.3 million for the year ended December 31, 2019 from $1.5 million during the period from January 18, 2018 (inception) to December 31, 2018. The increase was primarily due to an increase of $1.9 million in professional and accounting consulting service fees incurred in connection with our preparation to become a public company, an increase of $1.6 million in personnel-related costs, including share-based compensation, driven by an increase in headcount and an increase of $0.3 million in insurance related costs.

Other Expenses (Income), Net

Other expenses (income), net increased by $29.6 million to $30.6 million for the year ended December 31, 2019 from $1.0 million during the period from January 18, 2018 (inception) to December 31, 2018. The increase in other expenses was primarily due to the revaluation of our convertible preferred stock liability.

Liquidity and Capital Resources

To date, we have incurred significant net losses and negative cash flows from operations. As of December 31, 2019, we had available cash and cash equivalents of $93.3 million and an accumulated deficit of $73.6 million. Prior to our IPO, we funded our operations from the issuance and sale of capital stock. In connection with our IPO, we issued and sold an aggregate of 6,100,390 shares of common stock (inclusive of 795,703 shares of common stock from the exercise of the option to purchase additional shares granted to the underwriters) at a price of $16.00 per share. We received proceeds of $87.7 million, net of underwriting discounts and commissions and estimated offering costs.

Our primary use of cash is to fund operating expenses, which consist primarily of research and development expenditures related to our lead product candidate, BIO89-100. We plan to increase our research and development expenses substantially for the foreseeable future as we continue the clinical development of our current and future product candidates. At this time, due to the inherently unpredictable nature of clinical development, we cannot reasonably estimate the costs we will incur and the timelines that will be required to complete development, obtain marketing approval, and commercialize our current product candidate or any future product candidates. For the same reasons, we are also unable to predict when, if ever, we will generate revenue from product sales or our current or any future license agreements which we may enter into or whether, or when, if ever, we may achieve profitability. Clinical and preclinical development timelines, the probability of success, and development costs can differ materially from expectations. In addition, we cannot forecast the timing and amounts of milestone, royalty and other revenue from licensing activities, which future product candidates may be subject to future collaborations, when such arrangements will be secured, if at all, and to what degree such arrangements would affect our development plans and capital requirements.

Based on our research and development plans, we expect that our existing cash and cash equivalents will be sufficient to fund our operations into the second half of 2021. However, our operating plans and other demands on our cash resources may change as a result of many factors, and we may seek additional funds sooner than planned. There can be no assurance that we will be successful in acquiring additional funding at levels sufficient to fund our operations or on terms favorable to us.

Our future funding requirements will depend on many factors, including the following:

- the progress, timing, scope, results and costs of our clinical trials of BIO89-100 and preclinical studies or clinical trials of other potential product candidates we may choose to pursue in the future, including the ability to enroll patients in a timely manner for our clinical trials;
- the costs and timing of obtaining clinical and commercial supplies and validating the commercial manufacturing process for BIO89-100 and any other product candidates we may identify and develop;
- the cost, timing and outcomes of regulatory approvals;
- the timing and amount of any milestone, royalty or other payments we are required to make pursuant to current or any future collaboration or license agreements;
- costs of acquiring or in-licensing other product candidates and technologies;
- the terms and timing of establishing and maintaining collaborations, licenses and other similar arrangements;
- the costs associated with attracting, hiring and retaining additional qualified personnel as our business grows;
- our efforts to enhance operational systems and hire additional personnel to satisfy our obligations as a public company, including enhanced internal controls over financial reporting; and
- the cost of preparing, filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights.

We expect to continue to generate substantial operating losses for the foreseeable future as we expand our research and development activities. We will continue to fund our operations primarily through utilization of our current financial resources and through additional raises of capital to advance our current product candidate through clinical development, to develop, acquire or in-license other potential product candidates and to fund operations for the foreseeable future. However, there is no assurance that such funding will be available to us or that it will be obtained on terms favorable to us or will provide us with sufficient funds to meet our objectives. Any failure to raise capital as and when needed could have a negative impact on our financial condition and on our ability to pursue our business plans and strategies.

To the extent that we raise additional capital through partnerships or licensing arrangements with third parties, we may have to relinquish valuable rights to our product candidates, future revenue streams or research programs or to grant licenses on terms that may not be favorable to us. If we raise additional capital through public or private equity offerings, the ownership interest of our then-existing stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights. If we raise additional capital through debt financing, we may be subject to covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we are unable to obtain adequate financing when needed, we may have to delay, reduce the scope of or suspend one or more of our clinical trials or preclinical studies, research and development programs or commercialization efforts or grant rights to develop and market our product candidates even if we would otherwise prefer to develop and market such product candidates ourselves.

Cash Flows

The following table summarizes our cash flows for the periods presented (in thousands):

	Year Ended December 31, 2019	Period from January 18, 2018 (inception) to December 31, 2018
Net cash used in operating activities	$ (25,460)	$ (12,469)
Net cash used in investing activities	(139)	(39)
Net cash provided by financing activities	107,702	23,765
Net increase in cash and cash equivalents, and restricted cash	$ 82,103	$ 11,257

Net Cash Used in Operating Activities

During the year ended December 31, 2019, net cash used in operating activities was $25.5 million, which consisted of a net loss of $57.4 million, partially offset by non-cash charges of $31.0 million and a net change of $0.9 million in our net operating assets and liabilities. The non-cash charges are primarily comprised of the revaluation of our convertible preferred stock liability of $30.6 million and $0.4 million in share-based compensation. The change in our operating assets and liabilities was primarily due to a $2.9 million increase in accounts payable and accrued expenses as we grew our operations, partially offset by a $2.0 million increase in other current assets and other assets due to the timing of payments.

During the period from January 18, 2018 (inception) to December 31, 2018, net cash used in operating activities was $12.5 million, which consisted of a net loss of $16.2 million, partially offset by non-cash charges of $1.1 million and a net change of $2.6 million in our net operating assets and liabilities. The non-cash charges are primarily comprised of the revaluation of our convertible preferred stock liability of $1.0 million and $0.1 million in share-based compensation. The change in our net operating assets and liabilities was primarily due to a $2.7 million increase in accounts payable and accrued expenses as we grew our operations.

Net Cash Used in Investing Activities

During the year ended December 31, 2019 and the period from January 18, 2018 (inception) to December 31, 2018, net cash used in investing activities consisted of purchases of fixed assets.

Net Cash Provided by Financing Activities

During the year ended December 31, 2019 net cash provided by financing activities was $107.7 million, which consisted of net proceeds of $87.7 million received from our initial public offering and net proceeds of $20.0 million received from the issuance and sale of our convertible preferred stock.

During the period from January 18 (inception) to December 31, 2018 net cash provided by financing activities was $23.8 million, which primarily consisted of net proceeds of $23.7 million from the issuance and sale of our convertible preferred stock.

Contractual Obligations and Other Commitments

We are a smaller reporting company, as defined by Rule 12b-2 under the Securities and Exchange Act of 1934 and in Item 10(f)(1) of Regulation S-K, and are not required to provide the information under this item.

Off-Balance Sheet Arrangements

We have not entered into any off-balance sheet arrangements, as defined in the rules and regulations of the SEC, and do not have any holdings in variable interest entities.

Critical Accounting Polices and Estimates

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

While our significant accounting policies are described in the notes to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K, we believe that the following critical accounting policies are most important to understanding and evaluating our reported financial results.

Accrued Research and Development Expenses

We record accrued expenses for estimated preclinical and clinical trial and research expenses related to the services performed but not yet invoiced pursuant to contracts with research institutions, contract research organizations and clinical manufacturing organizations that conduct and manage preclinical studies, and clinical trials, and research services on our behalf. Payments for these services are based on the terms of individual agreements and payment timing may differ significantly from the period in which the services were performed. Our estimates are based on factors such as the work completed, including the level of patient enrollment. We monitor patient enrollment levels and related activity to the extent reasonably possible and make judgments and estimates in determining the accrued balance in each reporting period. Our estimates of accrued expenses are based on the facts and circumstances known at the time. If we underestimate or overestimate the level of services performed or the costs of these services, our actual expenses could differ from our estimates. As actual costs become known, we adjust our accrued expenses. To date, we have not experienced significant changes in our estimates of preclinical studies and clinical trial accruals.

Convertible Preferred Stock Liability

The freestanding instruments related to the commitments by the Series A convertible preferred shareholders to purchase and by us to sell our Series A convertible preferred shares in subsequent closings, contingent upon the achievement of certain developmental milestones and approval by the board of directors, at a fixed price per share, were considered a liability (or an asset) measured at fair value as the shares underlying the rights contain liquidation preferences upon certain "deemed liquidation events" that were not solely within the Company's control and which were considered in-substance contingent redemption features. The instruments were subject to revaluation at each balance sheet date until settlement or extinguishment, with revaluations recognized as a component of either other expenses (income), net in the consolidated statements of operations and comprehensive loss, or additional paid-in capital in the consolidated balance sheets.

Share-Based Compensation

We recognize compensation expense related to share-based awards granted to employees, directors, and non-employee service providers, including stock options, based on the estimated fair value of the awards on the date of grant. We estimate the grant date fair value, and the resulting share-based compensation, using the Black-Scholes option-pricing model. The grant date fair value of the share-based awards, which have graded vesting, is recognized using the straight-line method over the requisite service period of each award, which is generally the vesting period of the respective awards. We recognize forfeitures as they occur.

We use the Black-Scholes option-pricing model to estimate the fair value of stock option awards that requires the use of subjective assumptions to determine the fair value of share-based awards. These assumptions include:

- Expected volatility—Since we have limited trading history for our common stock due to our short trading history, the expected volatility was estimated based on the average volatility for comparable publicly traded biotechnology companies during the equivalent period of the calculated expected term of the options granted. The comparable companies were chosen based on their similar size, stage in the life cycle or area of specialty.
- Risk-free interest rate—The risk-free interest rate is based on the U.S. Treasury zero coupon bonds in effect at the time of grant for periods corresponding with the expected term of the option.
- Expected term—The expected term of options granted to employees and directors is determined using the "simplified" method. Under this approach, the expected term is presumed to be the mid-point between the weighted-average vesting term and the contractual term of the option. The simplified method makes the assumption that the employee will exercise share options evenly over the period when the share options are vested and ending on the date when the share options would expire. The expected option term for options granted to non-employees is based on the contractual term.
- Expected dividend—We have never paid dividends on our shares of common stock and have no plans to pay dividends on our shares of common stock. Therefore, we used an expected dividend of zero.

We will continue to use judgment in evaluating the expected volatility and expected term utilized for our share-based compensation calculations on a prospective basis.

Assumptions we used in applying the Black-Scholes option-pricing model to determine the estimated fair value of our stock options granted involve inherent uncertainties and the application of significant judgment. As a result, if factors or expected outcomes change and we use significantly different assumptions or estimates, our equity-based compensation could be materially different.

Prior to our IPO, given the absence of a public trading market for our shares of common stock, our board of directors exercised their judgment and considered a number of objective and subjective factors to determine the best estimate of the fair value of our shares of common stock, including timely valuations of our shares of common stock prepared by an unrelated third-party valuation firm, important developments in our operations, sales of convertible preferred shares, actual operating results and financial performance, the conditions in the biotechnology industry and the economy in general, the stock price performance and volatility of comparable public companies, and the lack of liquidity of our shares of common stock, among other factors. Following our IPO, the closing price per share of our common stock as reported on The Nasdaq Global Market on the date of grant is used to determine the determine the fair value of each share of common stock. Options granted shall be exercisable at a price per share not less than the estimated per share fair value of shares of common stock underlying those options on the date of grant.

Recent Accounting Pronouncements

See Note 2 to our consolidated financial statements appearing under Part II, Item 8 for more information about recent accounting pronouncements, the timing of their adoption, and our assessment, to the extent we have made one yet, of their potential impact on our financial condition of results of operations.

JOBS Act Accounting Election

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

We have elected to use this extended transition period to enable us to comply with new or revised accounting standards that have different effective dates for public and private companies 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 consolidated financial statements and our interim consolidated financial statements may not be comparable to companies that comply with new or revised accounting pronouncements.

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

We are a smaller reporting company, as defined by Rule 12b-2 under the Securities and Exchange Act of 1934 and in Item 10(f)(1) of Regulation S-K, and are not required to provide the information under this item.

Item 8. Financial Statements and Supplementary Data.

89BIO, INC.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the stockholders and the Board of Directors of 89bio, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheet of 89bio, Inc. and subsidiaries (the "Company") as of December 31, 2019, the related consolidated statements of operations and comprehensive loss, convertible preferred stock and stockholders' equity (deficit), and cash flows, for the year then ended, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2019, and the results of its operations and its cash flows for the year ended December 31, 2019, in conformity with accounting principles generally accepted in the United States of America.

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 audit. 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 audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether 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 audit, 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 audit 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 audit 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 audit provides a reasonable basis for our opinion.

/s/ Deloitte & Touche LLP

San Francisco, California
March 18, 2020

We have served as the Company's auditor since 2019.

Report of Independent Registered Public Accounting Firm

To the stockholders and the Board of Directors of 89bio, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheet of 89bio, Inc. and subsidiaries (operating as 89Bio Ltd. prior to the reorganization described in Note 1) (the "Company") as of December 31, 2018 and the related consolidated statements of operations and comprehensive loss, convertible preferred shares and shareholders' deficit and cash flows for the period from January 18, 2018 (inception) to December 31, 2018, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2018, and the results of its operations and its cash flow for the period from January 18, 2018 (inception) to December 31, 2018, in conformity with accounting principles generally accepted in the United States of America.

Going Concern

The 2018 financial statements were prepared assuming that the Company will continue as a going concern. As of the date of issuance of the Company's 2018 financial statements, the Company's lack of revenues and substantial operating losses raised substantial doubt about its ability to continue as a going concern. The 2018 financial statements did not include any adjustments that might result from the outcome of these uncertainties.

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 audit. 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 audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether 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 audit, 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 audit 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 audit 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 audit provides a reasonable basis for our opinion.

/s/ Brightman Almagor Zohar & Co.
Certified Public Accountants
A Firm in the Deloitte Global Network

Tel Aviv, Israel
August 15, 2019, except for the retroactive effect of both the 1-for-6.217 reverse stock split and the reorganization, as described in Note 1 as to which the date is October 28, 2019.

We have served as the Company's auditor since 2018. In 2019, we became the predecessor auditor.

89bio, Inc.
Consolidated Balance Sheets
(in thousands, except share and per share amounts)

	As of December 31,	
	2019	2018
Assets		
Current assets:		
Cash and cash equivalents	$ 93,335	$ 11,234
Restricted cash	25	23
Prepaid and other current assets	1,966	59
Total current assets	95,326	11,316
Property and equipment, net	155	33
Deferred tax assets	—	20
Other assets	72	—
Total assets	$ 95,553	$ 11,369
Liabilities, convertible preferred stock and stockholders' equity		
Current liabilities:		
Accounts payable	$ 989	$ 1,509
Accrued expenses	4,620	1,173
Convertible preferred stock liability	—	1,671
Total current liabilities	5,609	4,353
Commitments and contingencies (Note 5)		
Convertible preferred stock, $0.001 par value; 0 shares and 60,000,000 shares authorized as of December 31, 2019 and 2018, respectively; 0 shares and 24,000,000 shares issued and outstanding as of December 31, 2019 and 2018, respectively; liquidation value of $0 and $24,000 as of December 31, 2019 and 2018, respectively	—	23,073
Stockholders' equity (deficit):		
Common stock, $0.001 par value, 100,000,000 and 10,415,900 shares authorized as of December 31, 2019 and 2018, respectively; 13,788,982 and 611,226 shares issued and outstanding at December 31, 2019 and 2018, respectively	14	1
Additional paid-in capital	163,526	118
Accumulated deficit	(73,596)	(16,176)
Total stockholders' equity (deficit)	89,944	(16,057)
Total liabilities, convertible preferred stock and stockholders' equity	$ 95,553	$ 11,369

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

89bio, Inc.
Consolidated Statements of Operations and Comprehensive Loss
(In thousands, except share and per share amounts)

	Year Ended December 31, 2019	Period from January 18, 2018 (inception) to December 31, 2018
Operating expenses:		
Research and development	$ 21,346	$ 13,681
General and administrative	5,294	1,481
Total operating expenses	26,640	15,162
Loss from operations	26,640	15,162
Other expenses (income), net	30,562	986
Net loss before tax	57,202	16,148
Income tax expense	218	28
Net loss and comprehensive loss	$ 57,420	$ 16,176
Net loss per share, basic and diluted	$ 24.49	$ 36.45
Weighted-average shares used to compute net loss per share, basic and diluted	2,344,191	443,767

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

89bio, Inc.
Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)
(In thousands, except share data)

	Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amounts	Shares	Amounts			
Balance as of January 18, 2018 (inception)	—	$ —	—	$ —	$ —	$ —	$ —
Issuance of common stock	—	—	611,226	1	10	—	11
Issuance of convertible preferred stock, net of issuance costs of $235 and partial settlement of the convertible preferred stock liability of $692	23,900,000	22,973	—	—	—	—	—
Conversion of convertible note into preferred stock	100,000	100	—	—	—	—	—
Share-based compensation	—	—	—	—	108	—	108
Net loss and comprehensive loss	—	—	—	—	—	(16,176)	(16,176)
Balance as of December 31, 2018	24,000,000	$ 23,073	611,226	$ 1	$ 118	$ (16,176)	$ (16,057)
Issuance of convertible preferred stock, net of issuance costs of $0 and settlement of the convertible preferred stock liability of $6,673	20,000,000	26,673	—	—	—	—	—
Conversion of convertible preferred stock into common stock upon completion of initial public offering	(44,000,000)	(49,746)	7,077,366	7	49,739	—	49,746
Issuance of common stock in connection with the initial public offering, net of issuance costs of $3,083	—	—	6,100,390	6	87,685	—	87,691
Share-based compensation	—	—	—	—	389	—	389
Capital contribution related to extinguishment of preferred stock liability	—	—	—	—	25,595	—	25,595
Net loss and comprehensive loss	—	—	—	—	—	(57,420)	(57,420)
Balance as of December 31, 2019	—	$ —	13,788,982	$ 14	$ 163,526	$ (73,596)	$ 89,944

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

89bio, Inc.
Consolidated Statements of Cash Flows
(In thousands)

	Year Ended December 31, 2019	Period from January 18, 2018 (inception) to December 31, 2018
Cash flows from operating activities:		
Net loss	$ (57,420)	$ (16,176)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	17	6
Share-based compensation	389	108
Deferred tax assets	20	(20)
Revaluation of convertible preferred stock liability	30,597	979
Changes in operating assets and liabilities:		
Prepaids and other current assets	(1,918)	(48)
Other assets	(72)	—
Accounts payable	(520)	1,509
Accrued expenses	3,447	1,173
Net cash used in operating activities	(25,460)	(12,469)
Cash flows from investing activities:		
Purchases of property and equipment	(139)	(39)
Net cash used in investing activities	(139)	(39)
Cash flows from financing activities:		
Proceeds from issuance of convertible preferred stock and convertible preferred stock liability, net of issuance costs	20,000	23,665
Proceeds from issuance of common stock	11	—
Proceeds from issuance of convertible note	—	100
Proceeds from initial public offering net of issuance costs	87,691	—
Net cash provided by financing activities	107,702	23,765
Net increase in cash and cash equivalents, and restricted cash	82,103	11,257
Cash and cash equivalents, and restricted cash at beginning of year (period)	11,257	—
Cash and cash equivalents, and restricted cash at end of year (period)	$ 93,360	$ 11,257
Components of cash and cash equivalents, and restricted cash:		
Cash and cash equivalents	$ 93,335	$ 11,234
Restricted cash	25	23
Total cash and cash equivalents, and restricted cash	$ 93,360	$ 11,257
Supplemental disclosures of noncash information:		
Conversion of convertible note into preferred stock	$ —	$ 100
Conversion of convertible preferred stock into common stock at close of initial public offering	$ 49,746	$ —
Capital contribution related to extinguishment of preferred stock liability	$ 25,595	$ —
Property and equipment purchases included in accounts payable	$ 55	$ —
Cash paid for taxes	$ 106	$ —

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

1. Organization and Basis of Presentation

Description of Business

89bio, Inc. ("89bio" or the "Company") is a clinical-stage biopharmaceutical company focused on the development and commercialization of innovative therapies for the treatment of liver and cardio-metabolic diseases. The Company's lead product candidate, BIO89-100, a specifically engineered glycoPEGylated analog of fibroblast growth factor 21, is currently being developed for the treatment of nonalcoholic steatohepatitis.

89Bio Ltd. was incorporated in Israel in January 2018 and has two wholly owned subsidiaries: 89bio Management, Inc., located in San Francisco, California and UAB 89bio Lithuania, located in Vilnius, Lithuania. 89bio, Inc. was formed as a Delaware corporation on June 28, 2019, for the purpose of completing an initial public offering ("IPO") and related transactions in order to carry on the business of 89Bio Ltd.

The Company completed an internal reorganization transaction in September 2019, pursuant to which 89Bio Ltd. became a wholly owned subsidiary of 89bio, Inc. (the "Reorganization"). As part of the Reorganization, all of the equity holders of 89Bio Ltd. Exchanged 100% of the equity of 89Bio Ltd. for 100% of the equity of 89bio, Inc.

The Reorganization was considered a transaction between entities under common control. As a result, the accompanying consolidated financial statements have been retrospectively adjusted to reflect the Reorganization.

Initial Public Offering

On November 13, 2019, 89bio, Inc. completed the IPO, pursuant to which it issued and sold an aggregate of 6,100,390 shares of common stock (inclusive of 795,703 shares pursuant to the underwriters' option to purchase additional shares) at the IPO price of $16.00 per share, resulting in net proceeds of $87.7 million after deducting underwriting discounts and commissions of $6.8 million and other offering expenses of $3.1 million. Upon the closing of the IPO, the Company's outstanding convertible preferred stock automatically converted into 7,077,366 shares of common stock of 89bio, Inc. based on a proportional adjustment to the conversion ratio of the convertible preferred stock on a 1-for-6.217 basis.

Reverse Stock Split

On October 24, 2019, 89bio, Inc.'s board of directors approved an amendment to the amended and restated certificate of incorporation of 89bio, Inc. to effect a 1 for 6.217 reverse split ("Reverse Split") of shares of the common stock of 89bio, Inc. and a proportional adjustment to the conversion ratio of the convertible preferred stock, which was effected on October 25, 2019. The par value and authorized shares of common stock, and the par value, authorized and outstanding shares of the convertible preferred stock were not adjusted as a result of the Reverse Split. All of the share and per share information for 89bio, Inc. included in the accompanying consolidated financial statements has been adjusted to reflect the Reverse Split.

Liquidity

The accompanying consolidated financial statements have been prepared assuming the Company will continue as a going concern, which contemplates the realization of assets and liquidation of liabilities in the normal course of business. To date, the Company has not generated revenues from its activities and has incurred substantial operating losses. Management expects the Company to continue to generate substantial operating losses for the foreseeable future until it completes development of its products and seeks regulatory approvals to market such products. The Company had cash and cash equivalents of $93.3 million as of December 31, 2019. Management expects to continue to fund its operations primarily through utilization of its current financial resources and through additional raises of capital.

The Company intends to raise such capital through the issuance of additional equity financing and/or debt financing. However, if such financing is not available at adequate levels, the Company will need to reevaluate its operating plan and may be required to delay the development of its products. The Company expects that its cash and cash equivalents as of December 31, 2019 will be sufficient to fund operating expenses and capital expenditure requirements for a period of at least one year from the date these audited consolidated financial statements are filed with the Securities and Exchange Commission ("SEC").

2. Summary of Significant Accounting Policies

Basis of Presentation

The consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States ("U.S. GAAP").

Principles of Consolidation

The accompanying consolidated financial statements include the accounts of the Company and its wholly owned subsidiaries. All intercompany balances and transactions have been eliminated in consolidation.

Foreign Currencies

Certain transactions during the period from January 18, 2018 (inception) to December 31, 2018 and the year ended December 31, 2019 were denominated in the Euro or Israeli New Shekel. Gains and losses from foreign currency transactions were not material for all periods presented and are reflected in the consolidated statement of operations and comprehensive loss as a component of other expenses (income), net. The financial statements of UAB 89bio Lithuania use the Euro as the functional currency. The re-measurement from Euros to U.S. dollars results in translation gain and loss adjustments, which were not material for all periods presented. Accordingly, the Company has not presented translation gain and loss adjustments separately as a component of comprehensive loss.

Use of Estimates

The preparation of consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities as of the date of the consolidated financial statements and the reported amounts of expenses during the reporting period. Significant estimates and assumptions made in the accompanying consolidated financial statements include but are not limited to the fair value of stock options, the convertible preferred stock liability and certain accruals. The Company evaluates its estimates and assumptions on an ongoing basis using historical experience and other factors and adjusts those estimates and assumptions when facts and circumstances dictate. Actual results could differ from those estimates.

Fair Value Measurements

Financial assets and liabilities are recorded at fair value on a recurring basis in the balance sheets. The carrying values of Company's financial assets and liabilities, including cash and cash equivalents, restricted cash, prepaid and other current assets, accounts payable, and accrued expenses approximate to their fair value due to the short-term maturity of these instruments. Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability (an exit price) in an orderly transaction between market participants at the reporting date. Assets and liabilities recorded at fair value are categorized based upon the level of judgment associated with the inputs used to measure their fair value. Hierarchical levels are directly related to the amount of subjectivity with the inputs to the valuation of these assets or liabilities as follows:

Level 1—Observable inputs such as unadjusted, quoted prices in active markets for identical assets or liabilities at the measurement date;

Level 2—Inputs (other than quoted prices included in Level 1) are either directly or indirectly observable inputs for similar assets or liabilities. These include quoted prices for identical or similar assets or liabilities in active markets and quoted prices for identical or similar assets or liabilities in markets that are not active;

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.

Convertible Preferred Stock Liability

The freestanding instruments related to the commitment by the Series A convertible preferred stockholders to purchase and by the Company to sell its Series A convertible preferred stock in subsequent closings, contingent upon the achievement of certain developmental milestones and approval by the board of directors, at a fixed price per stock, were considered a liability (or an asset), measured at fair value as the shares underlying the rights contained liquidation preferences upon certain "deemed liquidation events" that were not solely within the Company's control and which were considered in-substance contingent redemption features (refer to Note 7 for further discussion on the redemption rights of the convertible preferred stock). The instruments were subject to revaluation at each balance sheet date until settlement or extinguishment, with revaluations recognized as either a component of other expenses (income), net in the consolidated statements of operations and comprehensive loss, or additional paid-in capital in the consolidated balance sheets.

Cash and Cash Equivalents and Restricted Cash

The Company considers all highly liquid investments purchased with original maturities of three months or less from the purchase date to be cash equivalents. Cash equivalents consist primarily of amounts invested in money market accounts and are stated at fair value. Restricted cash consists of a money market account that serves as collateral for the Company's operating lease agreement for its facility in Israel.

Concentrations of Credit Risk

Financial instruments that potentially subject the Company to a concentration of credit risk consist primarily of cash and cash equivalents. Bank deposits are held by accredited financial institutions and these deposits may at times be in excess of insured limits. The Company limits its credit risk associated with cash and cash equivalents by placing them with financial institutions that it believes are of high quality. The Company has not experienced any losses on its deposits of cash or cash equivalents.

Other Risks and Uncertainties

The Company's future results of operations involve a number of other risks and uncertainties. Factors that could affect the Company's future operating results and cause actual results to vary materially from expectations include, but are not limited to, the Company's early stages of clinical drug development; the Company's ability to advance product candidates into, and successfully complete, clinical trials on the timelines it projects; the Company's ability to adequately demonstrate sufficient safety and efficacy of its product candidates; the Company's ability to enroll patients in its ongoing and future clinical trials; the Company's ability to successfully manufacture and supply its product candidates for clinical trials; the Company's ability to obtain additional capital to finance its operations; uncertainties related to the projections of the size of patient populations suffering from the diseases the Company is targeting; the Company's ability to obtain, maintain, and protect its intellectual property rights; developments relating to the Company's competitors and its industry, including competing product candidates and therapies; general economic and market conditions; and other risks and uncertainties.

The Company's product candidates will require approvals from the U.S. Food and Drug Administration and comparable foreign regulatory agencies prior to commercial sales in their respective jurisdictions. There can be no assurance that any product candidates will receive the necessary approvals. If the Company was denied approval, approval was delayed or the Company was unable to maintain approval for any product candidate, it could have a materially adverse impact on the Company.

Property and Equipment, Net

Property and equipment are stated at cost, less accumulated depreciation. Depreciation is calculated on a straight-line basis over the estimated useful lives of the related assets, generally ranging from three to seven years. Leasehold improvements are amortized on a straight-line basis over the shorter of the assets' estimated useful life or the remaining term of the lease. Upon retirement or sale of the assets, the cost and related accumulated depreciation and amortization are removed from the balance sheet and the resulting gains or losses are recorded to the statements of operations. Maintenance and repair costs are expensed as incurred.

Impairment of Long-Lived Assets

The Company periodically evaluates its long-lived assets, including property and equipment, for impairment whenever events or changes in business circumstances indicate that the carrying amount of the assets or group of assets may not be fully recoverable. If indicators of impairment exist and the undiscounted future cash flows that the assets are expected to generate are less than the carrying value of the assets, the Company reduces the carrying amount of the assets through an impairment charge, to their estimated fair values based on a discounted cash flow approach or, when available and appropriate, to comparable market values. There were no such indicators for the periods presented.

Leases

The Company leases its office facilities under a non-cancelable operating lease agreement and recognizes related rent expense on a straight-line basis over the term of the lease.

Research and Development Expenses and Accrued Research and Development Expenses

Research and development expenses consist primarily of costs incurred for the development of the Company's lead product candidate, BIO89-100. Research and development expenses consist primarily of external costs related to acquiring and licensing patents and intellectual properties, preclinical and clinical development and related supplies, and personnel costs. Personnel costs consist of salaries, employee benefits and share-based compensation for individuals involved in research and development efforts. The Company estimates preclinical and clinical study and research expenses based on the services performed, pursuant to contracts with research institutions that conduct and manage preclinical and clinical studies and research services on its behalf. The Company records the costs of research and development activities based upon the estimated amount of services provided but not yet invoiced and includes these costs in accrued liabilities in the consolidated balance sheets. These costs are a component of the Company's research and development expenses.

The Company accrues for these costs based on factors such as estimates of the work completed and in accordance with agreements established with its third-party service providers under the service agreements. The Company makes significant judgments and estimates in determining the accrued liabilities balance. As actual costs become known, the Company adjusts its accrued expenses. The Company has not experienced any material differences between accrued costs and actual costs incurred. However, the status and timing of actual services performed may vary from the Company's estimates, resulting in adjustments to expense in future periods. Changes in these estimates that result in material changes to the Company's accruals could materially affect the Company's results of operations. Payments associated with licensing agreements to acquire licenses to develop, use, manufacture and commercialize products that have not reached technological feasibility and do not have alternate commercial use are expensed as incurred. Contingent milestone payments, if any, are expensed when the milestone results are probable and estimable, which is generally upon achievement of the milestone.

Share-Based Compensation

The Company measures its share-based payment awards made to employees, directors, and non-employee service providers based on estimated fair values and recognizes compensation over the requisite service period.

The Company estimates the fair value of share-based payment awards on the date of grant using a Black-Scholes option pricing model. The value of the portion of the share-based payment award that is ultimately expected to vest is recognized as an expense over the requisite service period in the consolidated statements of operations and comprehensive loss.

The Company recognizes compensation for the value of share-based payment awards, which have graded vesting, using the straight-line method over the requisite service period of each award. The Company accounts for forfeitures as they occur.

The Black-Scholes option pricing model requires a number of assumptions, of which the most significant are expected volatility, expected option term (the time from the grant date until the options are exercised or expire), risk-free rate, and expected divided rate. Expected volatility is estimated based on volatility of comparable publicly traded biotechnology companies. The Company has historically not paid dividends and has no foreseeable plans to pay dividends, therefore the Company uses an expected dividend yield of 0%. The risk-free interest rate is based on the yield from U.S. Treasury zero-coupon bonds with an equivalent expected term. The expected option term is calculated for options granted to employees and directors using the "simplified" method. Under this approach, the expected term is presumed to be the midpoint between the weighted average vesting term and the contractual term of the option. The simplified method makes the assumption that the employee will exercise share options evenly over the period when the share options are vested and ending on the date when the share options expire. The expected option term for options granted to non-employees is based on the contractual term. Changes in the determination of each of the inputs can affect the fair value of the share options granted and the results of operations of the Company.

Deferred Offering Costs

Deferred offering costs, consisting of legal, accounting, and filing fees directly relating to the IPO, were capitalized and upon completion of the IPO, approximately $3.1 million of deferred offering costs were offset against the IPO proceeds in additional paid-in capital. For the year ended December 31, 2018, the Company did not incur any deferred offering costs.

Income Taxes

Income taxes are accounted for under the asset and liability method. Under this method, deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the consolidated financial statements carrying amounts of existing assets and liabilities and their respective tax bases and operating loss and tax credit carryforwards. Deferred tax assets and liabilities are measured using enacted tax rates applied to taxable income in the years in which those temporary differences are expected to be realized. The effect on deferred tax assets and liabilities of a change in tax rates is recognized as income or loss in the period that includes the enactment date. A valuation allowance is established when necessary to reduce deferred tax assets to the amount expected to be realized. Interest and penalties related to unrecognized tax benefits are included within the provision of income tax. To date, there have been no unrecognized tax benefits balances.

Basic and Diluted Net Loss per Share

Basic loss per share is computed by dividing the net loss by the weighted average number of common stock outstanding during the period. Diluted loss per share is computed by dividing the net loss by the weighted average number of common stock outstanding together with the number of additional common stock that would have been outstanding if all potentially dilutive common stock had been issued. Since the Company was in a loss position for the periods presented, basic net loss per share is the same as diluted net loss per share since the effects of potentially dilutive securities are antidilutive.

Comprehensive Loss

The Company's comprehensive loss is comprised of changes related to translation gain and loss adjustments, which were not material for all periods presented. Accordingly, the Company has not presented comprehensive loss separately from net loss on the consolidated statements of operations and comprehensive loss.

Segment Reporting

The Company has one operating segment. The Company's chief operating decision maker, its Chief Executive Officer, manages the Company's operations on a consolidated basis for the purposes of allocating resources and evaluating financial performance.

Recently Adopted Accounting Standards

In May 2014, the Financial Accounting Standards Board (the "FASB") issued Accounting Standards Update ("ASU") 2014-09—*Revenue from contracts with customers*, to achieve a consistent application of revenue recognition, resulting in a single revenue model to be applied by reporting companies under U.S. GAAP. Under the new model, recognition of revenue occurs when a customer obtains control of the promised goods or services in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. In addition, the standard requires that reporting companies disclose the nature, amount, timing, and uncertainty of revenue and cash flows arising from contracts with customers. The standard is effective for public entities for fiscal years beginning after December 15, 2017 and is effective for nonpublic entities for fiscal years beginning after December 15, 2018. The standard is required to be applied retrospectively to each prior reporting period presented or retrospectively with the cumulative effect of initially applying it recognized at the date of initial application. The Company adopted this standard on January 1, 2019, and as the Company has no revenues to date, the adoption of the standard did not have any impact on its consolidated financial statements.

In June 2018, the FASB issued ASU No. 2018-07 *Compensation—Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting*, which is intended to reduce the cost and complexity and to improve financial reporting for nonemployee share based payment. The standard expands the scope of Topic 718, (which currently only includes share-based payments to employees) to include share-based payments issued to nonemployees for goods or services. Consequently, the accounting for share-based payments to nonemployees and employees will be substantially aligned. The standard is effective for public entities for fiscal years beginning after December 15, 2019 and nonpublic entities for fiscal years beginning after December 15, 2020. Early adoption is permitted but no earlier than a company's adoption date of Topic 606. The Company early adopted this standard on January 1, 2019, and the impact of its adoption on the Company's consolidated financial statements was not material.

Recent Accounting Pronouncements

In February 2016, the FASB issued ASU 2016-02—*Leases*, requiring the recognition of lease assets and liabilities on the balance sheet. The standard: (a) clarifies the definition of a lease; (b) requires a dual approach to lease classification similar to current lease classifications; and (c) causes lessees to recognize leases on the balance sheet as a lease liability with a corresponding right-of-use asset for leases with a lease-term of more than twelve months. The standard is effective for public entities for fiscal years beginning after December 15, 2018 and for nonpublic entities for fiscal years beginning after December 15, 2020. The Company is currently evaluating the impact of this standard on its consolidated financial statements and related disclosures.

In August 2018, the FASB issued ASU No. 2018-13, *Disclosure Framework – Changes to the Disclosure Requirements for Fair Value Measurement*, which amends ASC 820, Fair Value Measurement. This ASU modifies the disclosure requirements for fair value measurements by removing, modifying, or adding certain disclosures. The standard is effective for public and nonpublic entities for fiscal years beginning after December 15, 2019, with early adoption permitted for the removed disclosures and delayed adoption until fiscal years beginning after December 15, 2019 permitted for the new disclosures. The removed and modified disclosures will be adopted on a retrospective basis and the new disclosures will be adopted on a prospective basis. The Company is currently evaluating the impact of this standard on its consolidated financial statements and related disclosures.

In December 2019, the FASB issued ASU 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes* ("ASU 2019-12"), which is intended to simplify the accounting for income taxes. ASU 2019-12 removes certain exceptions to the general principles in Topic 740 and also clarifies and amends existing guidance to improve consistent application. The new standard is effective for public entities for fiscal years beginning after December 15, 2020 and for nonpublic entities for fiscal years beginning after December 15, 2021. The Company is currently evaluating the impact of this standard on its consolidated financial statements and related disclosures.

3. Fair Value Measurements

The fair value of the Company's financial liabilities measured at fair value on a recurring basis by level within the fair value hierarchy are as follows (in thousands):

	As of December 31, 2019			
	Level 1	Level 2	Level 3	Total
Liabilities:				
Convertible preferred stock liability	$ —	$ —	$ —	$ —
Total financial liabilities	$ —	$ —	$ —	$ —

	As of December 31, 2018			
	Level 1	Level 2	Level 3	Total
Liabilities:				
Convertible preferred stock liability	$ —	$ —	$ 1,671	$ 1,671
Total financial liabilities	$ —	$ —	$ 1,671	$ 1,671

The changes in the fair value of the Company's Level 3 financial liabilities, which are measured on a recurring basis are as follows (in thousands):

	As of December 31,	
	2019	2018
Beginning balance	$ 1,671	$ —
Recognition of convertible preferred stock liability upon issuance of convertible preferred stock	—	638
Revaluation of convertible preferred stock liability recorded in other expenses (income), net	30,597	979
Partial settlement of convertible preferred stock liability upon second closing	—	54
Partial settlement of convertible preferred stock liability upon third closing	(6,673)	—
Capital contribution related to extinguishment of preferred stock liability	(25,595)	—
Ending balance	$ —	$ 1,671

The Company's convertible preferred stock liability resulted from the initial sale of Series A convertible preferred stock where the investors' committed to purchase additional shares of Series A convertible preferred stock in subsequent closings, contingent upon the achievement by the Company of certain development milestones and approval by the board of directors. The investors' commitment to purchase and the Company's commitment to sell shares of Series A convertible preferred stock represented a freestanding instrument accounted for at fair value and re-measured at each reporting date. The Company estimated the fair value of this commitment using the Black Scholes option pricing model using the following assumptions:

	Year Ended December 31, 2019	Period from January 18, 2018 (inception) to December 31, 2018
Stock price	$0.99-$2.57	$0.96-$0.99
Exercise price	$ 1.00	$ 1.00
Expected term (years)	0.00-2.25	0.25-3.21
Expected volatility	72.0%	70.0-72.0%
Risk-free interest rate	0.0-2.4%	2.1-2.9%

The main factor impacting the change in fair value of the convertible preferred stock liability was the estimated stock price of the preferred stock liability. Refer to Note 7 for further discussion on the convertible preferred stock liability and the accounting upon extinguishment of the preferred stock liability.

4. Consolidated Balance Sheet Components

Property and Equipment, Net

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

	As of December 31,	
	2019	2018
Computer software and electronic equipment	$ 67	$ 33
Furniture and office equipment	111	6
Total property and equipment	178	39
Less: accumulated depreciation	(23)	(6)
Total property and equipment, net	$ 155	$ 33

Depreciation expense for property and equipment was $17,000 for the year ended December 31, 2019 and $6,000 for the period from January 18, 2018 (inception) to December 31, 2018.

Accrued Expenses

Accrued expenses consist of the following (in thousands):

	As of December 31,	
	2019	2018
Accrued research and development expenses	$ 2,326	$ 890
Accrued employee and related expenses	1,396	283
Accrued professional and legal fees	573	—
Accrued other	325	—
Total accrued expenses	$ 4,620	$ 1,173

5. Commitments and Contingencies

Leases

In May 2018, the Company entered into an operating lease agreement for its facility in Israel. The lease term was for 12 months and was amended in April 2019 to extend the lease term to April 2020. Under the lease agreement, monthly lease payments are approximately $4,000.

In December 2019, the Company entered into an operating lease for its headquarters in San Francisco. The lease term is for 24 months, expiring in January 2022, and monthly lease payments are approximately $17,500.

Future minimum lease payments under the Company’s non-cancellable operating lease obligations as of December 31, 2019, are as follows (in thousands):

2020	$ 226
2021	216
Total future minimum annual payments	$ 442

Rent expense was $159,000 for year ended December 31, 2019 and $39,000 during the period from January 18, 2018 (inception) to December 31, 2018. The Company has security deposit balances of $95,000, which are included in restricted cash and other assets in the consolidated balance sheets as of December 31, 2019. The security deposit balance of $23,000 was included in restricted cash in the consolidated balance sheets as of December 31, 2018.

Asset Transfer and License Agreement with Teva Pharmaceutical Industries Ltd

In April 2018, the Company concurrently entered into two Asset Transfer and License Agreements (the "Teva Agreements") with Teva Pharmaceutical Industries Ltd ("Teva") under which it acquired certain patents and intellectual property relating to two programs: (1) Teva's glycoPEGylated FGF21 program, including the compound TEV-47948 (BIO89-100), a glycoPEGylated long-acting FGF21 and (2) Teva's development program of small molecule inhibitors of Fatty Acid Synthase. Pursuant to the Teva Agreements, the Company paid Teva an initial nonrefundable upfront payment of $6.0 million and the Company could be obligated to pay Teva up to $67.5 million under each program, for a total of $135.0 million, upon the achievement of certain clinical development and commercial milestones. In addition, the Company is obligated to pay Teva tiered royalties at percentages in the low-to-mid single-digits on worldwide net sales on all products containing the Teva compounds.

The Teva Agreements can be terminated (i) by the Company without cause, after the first anniversary of the effective date, upon 120 days' written notice to Teva, (ii) by either party, if the other party materially breaches any of its obligations under the Agreements and fails to cure such breach within 60 days after receiving notice thereof, or (iii) by either party, if a bankruptcy petition is filed against the other party and is not dismissed within 60 days. In addition, Teva can also terminate the agreement related to the Company's glycoPEGylated FGF21 program in the event the Company, or any of its affiliates or sublicensees, challenges any of the Teva patents licensed to the Company, and the challenge is not withdrawn within 30 days of written notice from Teva.

The Company accounted for the acquisition of technology as an asset acquisition because it did not meet the definition of a business. The Company recorded the total consideration transferred to Teva as research and development expense in the consolidated statements of operations and comprehensive loss because the acquired technology represented in-process research and development and had no alternative future use. During the period from January 18, 2018 (inception) to December 31, 2018, the Company recognized an up-front license payment of $6.0 million in research and development expenses under the Teva Agreements in its consolidated statements of operations and there were no such license payment expenses related to the Teva Agreements during the year ended December 31, 2019.

6. Convertible Note

In March 2018, the Company entered into a Convertible Loan Agreement (the "Convertible Note") with a principal amount of $100,000 and a fixed interest rate of 8% per annum. The Convertible Note was automatically convertible into the Company's next equity financing, or upon an earlier event of default. In April 2018, the entire amount outstanding converted into 100,000 shares of Series A convertible preferred stock upon the initial closing of the Series A financing.

7. Convertible Preferred Stock

In April 2018, the Company entered into the Series A Share Purchase Agreement (the " Series A SPA"), pursuant to which the investors committed to invest an aggregate amount of up to $60.0 million for the issuance of shares of Series A convertible preferred stock at a price of $1.00 per share.

The initial closing occurred on April 16, 2018, and the Company issued 14,900,000 shares of Series A convertible preferred stock at a price per share of $1.00 for net cash proceeds of $14.7 million. The investors also committed to purchase 15,000,000 and 30,000,000 shares of Series A convertible preferred stock at a price of $1.00 per share in second and third closings, respectively, contingent upon the achievement by the Company of certain development milestones and approval by the board of directors.

The investors' commitment to purchase and the Company's commitment to sell shares of Series A convertible preferred stock represent a freestanding instrument accounted for at fair value and re-measured at each reporting date. The Company estimates the fair value of this commitment using the Black-Scholes option pricing model. On the date of the initial closing, the Company recorded the commitments associated with the second and third closings of the Series A convertible preferred stock at a net value of $638,000. For the year ended December 31, 2019 and for the period from January 18, 2018 (inception) to December 31, 2018, the Company recorded an expense of $30.6 million and $1.0 million, respectively, for the revaluation of the convertible preferred stock liability, within other expenses (income), net in the consolidated statements of operations and comprehensive loss.

In December 2018, the Series A convertible preferred stockholders partially accelerated the second closing and the Company issued 9,000,000 shares of Series A convertible preferred stock at a price of $1.00 per share and received net proceeds of $9.0 million.

In June 2019, the Company and the Series A convertible preferred stockholders agreed to issue the remaining 6,000,000 shares of Series A convertible preferred stock at a price of $1.00 per share related to the second closing, and to partially accelerate 14,000,000 shares of Series A convertible preferred stock at a price of $1.00 per share related to the third closing. The shares were issued and the aggregate net proceeds of $20.0 million were received in June and July 2019.

In September 2019, the Company completed an internal reorganization transaction pursuant to which 89Bio Ltd. became a wholly owned subsidiary of 89bio, Inc. As part of the Reorganization, all outstanding convertible preferred shares of 89Bio Ltd. were exchanged into shares of convertible preferred stock of 89bio, Inc.

On October 25, 2019, the Company and the Series A preferred stockholders amended the Series A SPA, and the parties agreed that the Series A SPA would terminate upon consummation of the Company's IPO.

Upon the completion of the Company's IPO on November 13, 2019, the remaining 16,000,000 shares of convertible preferred stock that were previously issuable under the third closing were no longer issuable. Accordingly, the preferred stock liability was extinguished and because the transaction occurred between related parties, the resulting $25.6 million was accounted for as a capital contribution by the preferred stockholders.

Additionally, immediately prior to the completion of the Company's IPO, all outstanding shares of convertible preferred stock automatically converted into 7,077,366 shares of common stock and the related carrying value was reclassified to common stock and additional paid-in capital. Accordingly, there were no shares of convertible preferred stock outstanding as of December 31, 2019.

Convertible preferred stock as of December 31, 2018 consisted of the following:

	Shares Authorized	Shares Issued and Outstanding	Carrying Value	Liquidation Value
Series A	60,000,000	24,000,000	$ 23,073,000	$ 24,000,000
Total	60,000,000	24,000,000	$ 23,073,000	$ 24,000,000

The Company's certificate of incorporation did not provide redemption rights to the holders of the Series A convertible preferred stock. In the event of a liquidation event, all the funds and assets of the Company available for distribution among all the stockholders would be distributed in the following order of preference: (a) the holders of the Series A convertible preferred stock would be entitled to receive an amount per share equal to $1.00 per each Series A convertible preferred stock (less the amount of distributions actually received in any prior liquidation event, plus all declared but unpaid dividends) and (b) the remaining assets of the Company available for distribution to stockholders would be distributed among the holders of common stock and to the holders of the Series A convertible preferred stock on an as-converted and pro rata basis.

Although the convertible preferred stock was not redeemable, in the event of certain "deemed liquidation events" that were not solely within the Company's control (including merger, acquisition, or sale of all or substantially all of the Company's assets), the holders of the convertible preferred stock would be entitled to preference amounts paid before distribution to other stockholders and hence effectively redeeming the preference amount. As of December 31, 2018, the convertible preferred stock was classified outside of stockholders' equity (deficit) as a result of these in-substance contingent redemption rights and the Company did not adjust the carrying values of the convertible preferred stock to the deemed liquidation values of such shares since a liquidation event was not probable of occurring.

8. Common Stock

The Company is authorized to issue a total of 100,000,000 shares of common stock with a par value of $0.001 per share, 13,788,982 of which were issued and outstanding as of December 31, 2019.

Total common stock reserved for issuance is summarized as follows:

	As of December 31,	
	2019	2018
Series A convertible preferred stock outstanding, as converted	—	3,860,383
Options issued and outstanding	1,320,243	591,448
Shares available for future option grants	1,523,950	472,714
Total common stock reserved for issuance	2,844,193	4,924,545

9. Share-Based Compensation

Equity Incentive Plans

In 2018, the Company's board of directors adopted the 89Bio Ltd. 2018 Equity Incentive Plan (the "2018 Plan"). In connection with the Reorganization, in September 2019, the Company's board of directors approved the 2019 Equity Incentive Plan (the "2019 Plan"), which became effective on September 17, 2019. From and after the effective date of the 2019 Plan, the Company will no longer be making any future awards under the 2018 Plan.

The Company initially reserved 2,844,193 shares of common stock for issuance under the 2019 Plan. In addition, the number of shares of common stock reserved for issuance under the 2019 Plan will automatically increase on the first day of January for a period of up to ten years, commencing on January 1, 2020, in an amount equal to 4% of the total number of shares of the Company's capital stock outstanding on the immediately preceding December 31, or a lesser number of shares determined by the Company's board of directors. As of December 31, 2019, there were 1,523,950 shares of common stock available for issuance as future option grants under the 2019 Plan.

The Board determines the period over which options become exercisable and options generally vest over a four-year period, with 25% of options vesting on the first anniversary of employment, and thereafter, the remaining options vesting quarterly, over the following 36-month period. The options will expire within ten years from the date of grant. The exercise price of awards granted will not be less than the estimated fair value of the shares on the date of grant.

Employees Share Purchase Plan (ESPP)

In October 2019, the Company adopted the 2019 Employee Stock Purchase Plan ("ESPP"), which became effective following the date of the IPO. The Company initially reserved 225,188 shares of common stock for purchase under the ESPP. The number of shares of common stock reserved for issuance under the 2019 ESPP will automatically increase on the first day of January for a period of up to ten years, in an amount equal to 1% of the total number of shares of the Company's common stock outstanding on the immediately preceding December 31, or a lesser number of shares determined by the Company's board of directors. Purchases will be accomplished through the participation of discrete offering periods. Each offering will be no more than 27 months long. For each offering period, ESPP participants will purchase shares of common stock at a price per share equal to 85% of the lesser of the fair market value of the Company's common stock on (1) the first trading day of the applicable offering period or (2) the last trading day of each purchase period the applicable offering period.

As of December 31, 2019, no offering periods have commenced under the ESPP and 225,188 shares of common stock remained available for issuance under the ESPP.

The Company recorded share-based compensation for the periods indicated as follows (in thousands):

	Year Ended December 31, 2019	Period from January 18, 2018 (inception) to December 31, 2018
Research and development	$ 30	$ 13
General and administrative	359	95
Total share-based compensation	$ 389	$ 108

The fair value of option awards granted for the periods indicated was estimated at the date of grant using a Black-Scholes option-pricing model with the following assumptions:

	Year Ended December 31, 2019	Period from January 18, 2018 (inception) to December 31, 2018
Expected term (years)	5.88-6.11	5.9
Expected volatility	61.8-87.6%	73.2%
Risk-free interest rate	1.6-2.6%	3.1%
Expected dividend	—	—

The following table summarizes stock option activity under the 2019 Plan:

	Number of Options	Weighted Average Exercise Price	Weighted Average Remaining Contractual Term (In years)	Aggregate Intrinsic Value (In thousands)
Balance outstanding as of December 31, 2018	591,448	$ 1.93	9.87	$ —
Granted	742,285	4.37		
Exercised	—	—		
Cancelled	(13,490)	1.93		
Balance outstanding as of December 31, 2019	1,320,243	$ 3.34	9.23	$ 30,353
Exercisable as of December 31, 2019	235,188			$ 5,730

During the year ended December 31, 2019, the estimated total grant date fair value of options vested was $296,000. Options granted for the period from January 18, 2018 (inception) to December 31, 2018 were subject to cliff vesting as of December 31, 2018, and accordingly, there were no vested options during the period. The weighted-average grant date fair value of options granted for the year ended December 31, 2019 and for period from January 18, 2018 (inception) to December 31, 2018 was $2.90 and $1.31 per share, respectively. As of December 31, 2019, there was $2.4 million of unrecognized share-based compensation cost related to stock options granted under the 2019 Plan, which is expected to be recognized over a weighted-average period of 3.40 years.

Included in the option activity table are 3,216 stock options granted to non-employee service providers during the year ended December 31, 2019. These options were granted in exchange for consulting services to be rendered and vest over the term specified in the grant. Non-employee share-based compensation was immaterial during the year ended December 31, 2019.

10. Income Taxes

Tax Rates Applicable to the Income of the Company and its Subsidiaries

As a result of the Reorganization described in Note 1, as of December 31, 2019, the Company is taxed according to U.S. federal and state tax laws and Israeli tax laws. Prior to the Reorganization, for the year ended December 31, 2018, the Company was taxed according to Israeli tax laws. The statutory tax rates applicable to the income of the Company and its subsidiaries are as follows:

	Year Ended December 31, 2019	Period from January 18, 2018 (inception) to December 31, 2018
89bio, Inc.	21%	—
89Bio Ltd	23%	23%
89bio Management, Inc.	21%	21%
UAB 89bio Lithuania	15%	15%

The expense for income taxes is comprised of (in thousands):

	Year Ended December 31, 2019	Period from January 18, 2018 (inception) to December 31, 2018
Current:		
Federal	$ 167	$ —
State	1	—
Foreign	30	48
Total	198	48
Deferred:		
Federal	20	—
State	—	—
Foreign	—	(20)
Total	20	(20)
Income tax expense	$ 218	$ 28

Deferred Income Taxes

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Significant components of the Company's deferred tax assets are as follows (in thousands):

	As of December 31,	
	2019	2018
Israel net operating loss carryforwards	$ 4,328	$ 1,536
U.S. net operating loss carryforwards	1,916	—
Research and development expenses	3,327	1,966
Other	451	20
Total deferred tax assets	10,022	3,522
Less: valuation allowance	(10,022)	(3,502)
Net deferred tax assets	$ —	$ 20

As of December 31, 2019 and 2018, the Company recorded a valuation allowance of $10.0 million and $3.5 million, respectively, in respect of deferred tax assets resulting from tax loss carryforwards and other temporary differences. Realization of deferred tax assets is dependent upon future earnings, if any, the time and amount of which are uncertain. As the Company is still in its development stage and has not yet generated revenues, it is more likely than not that sufficient taxable income will not be available for the tax losses to be utilized in the future. Therefore, a valuation allowance was recorded to reduce the deferred tax assets to their recoverable amounts. The valuation allowance increased by $6.5 million in 2019, which primarily relates to significant taxable losses. It also includes a recapture of the valuation allowance against the Company's deferred tax assets in the United States due to the reorganization that occurred in 2019, which increased the valuation allowance by $20,000.

Available Carryforward Tax Losses and Credits

As of December 31, 2019, the Company has an accumulated tax loss carryforward of approximately $9.1 million and $23.8 million for U.S. and Israeli tax purposes, respectively. For the period from January 18, 2018 (inception) to December 31, 2018, the Company had an accumulated tax loss carryforward of approximately $6.7 million for Israeli tax purposes. Federal net operating losses generated after 2017 can be carried forward indefinitely but utilization will be limited to 80% of taxable income in the period that net operating losses are being utilized. Carryforward tax losses in Israel have no expiration date.

As of December 31, 2019, the Company has state research and development credit carryforwards of approximately $156,000, which will carryforward indefinitely.

Loss from Continuing Operations, Before Taxes on Income

The Company recorded a loss from continuing operations, before taxes on income for the periods indicated as follows (in thousands):

	Year Ended December 31, 2019	Period from January 18, 2018 (inception) to December 31, 2018
United States	$ (19,502)	$ 50
Lithuania	200	50
Israel	(37,900)	(16,248)
Net loss before tax	$ (57,202)	$ (16,148)

Reconciliation of Income Tax Expense

The reconciliation of income tax expense based on the statutory tax rate to the effective tax rate is as follows (in thousands):

	Year Ended December 31, 2019	Period from January 18, 2018 (inception) to December 31, 2018
Income tax expense computed at statutory rates	$ (13,095)	$ (3,714)
Change in valuation allowance	6,520	3,502
Change in Israel effective tax rate due to the 2019 reorganization	734	—
Revaluation of convertible preferred share liability	6,039	226
Other	20	14
Income tax expense	$ 218	$ 28

Utilization of the U.S. federal and state net operating losses and credit carryforwards may be subject to an annual limitation provided for in Section 382 of the Internal Revenue Code and similar state codes. Any annual limitation could result in a deferral of the utilization of the net operating loss and credit carryforwards.

Unrecognized Tax Benefits

During the year ended December 31, 2019, the amount of gross unrecognized tax benefits increased by $39,000 from a balance at the beginning of the year of $0. If the total amount of unrecognized tax benefits was recognized, it would not have an impact to the effective tax rate as it would be offset by the reversal of related deferred tax assets which are subject to a full valuation allowance.

The Company recognizes interest and penalties related to uncertain tax positions as part of the income tax provision. As of December 31, 2019 and 2018, such interest and penalties have not been material.

The Company is subject to taxation in the United States, California and several foreign jurisdictions. To date, the Company has not been subject to any federal or state income tax audits. As of December 31, 2019, all tax years remain open to examination.

11. Net Loss Per Share

The following outstanding potentially dilutive common stock equivalents have been excluded from the calculation of diluted net loss per share for the periods presented due to their anti-dilutive effect:

	Year Ended December 31, 2019	Period from January 18, 2018 (inception) to December 31, 2018
Convertible preferred stock, as converted	—	3,860,383
Stock options to purchase common stock	1,320,243	591,448
Shares available for future option grants	1,523,950	472,714
Total	2,844,193	4,924,545

12. Related Party Transactions

The Company incurred $170,000 and $147,000 in professional consulting services expense related to certain members of the board of directors for the year ended December 31, 2019 and for the period from January 18, 2018 (inception) to December 31, 2018, respectively, which were recorded within research and development expenses on the Company's consolidated statements of operations and comprehensive loss. The related party liability balance was $11,000 and $23,000 as of December 31, 2019 and 2018, respectively, which was recorded within accounts payable and accrued expenses on the Company's consolidated balance sheets.

The Company and the Series A preferred stockholders amended the Series A SPA on October 25, 2019, and the parties agreed that the Series A SPA would terminate upon consummation of the Company's IPO. Upon the completion of the Company's IPO on November 13, 2019, the remaining 16,000,000 shares of convertible preferred stock that were issuable were no longer issuable. Accordingly, the preferred stock liability was extinguished and because the transaction occurred between related parties, the resulting $25.6 million was accounted for as a capital contribution by the preferred stockholders and recorded as part of additional paid-in capital on the consolidated balance sheets (see Note 7).

13. Selected Quarterly Financial Data (Unaudited)

Selected quarterly results from operations for the year ended December 31, 2019 is as follows:

	Three Months Ended,			
	December 31,	September 30,	June 30,	March 31,
	(in thousands, except per share data)			
2019				
Loss from operations	$ (9,611)	$ (8,198)	$ (3,947)	$ (4,884)
Net loss and comprehensive loss	(19,283)	(18,725)	(14,525)	(4,887)
Net loss per share, basic and diluted	$ (2.58)	$ (30.63)	$ (23.76)	$ (8.00)

Selected quarterly results from operations for the period from January 18, 2018 (inception) to December 31, 2018 is as follows:

	Three Months Ended,			Period from January 18, 2018 (inception) to
	December 31,	September 30,	June 30,	March 31,
	(in thousands, except per share data)			
2018				
Loss from operations	$ (4,408)	$ (3,786)	$ (6,968)	$ —
Net loss and comprehensive loss	(4,638)	(4,165)	(7,373)	—
Net loss per share, basic and diluted	$ (7.59)	$ (6.81)	$ (13.55)	$ —

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, our management, with the participation and supervision of our principal executive officer and our principal financial officer, evaluated our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act). The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the Company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost benefit relationship of possible controls and procedures. Based on this evaluation, our principal executive officer and our principal financial officer concluded that solely as a result of the material weaknesses in our internal control over financial reporting described below, our disclosure controls and procedures were not effective as of December 31, 2019 to provide reasonable assurance that information we are required to disclose in reports that we file or submit under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified in SEC rules and forms, and that such information is accumulated and communicated to our management, including our principal executive officer and our principal financial officer, as appropriate, to allow timely decisions regarding required disclosure.

Remediation Efforts on Previously Reported Material Weaknesses

During the audit of our consolidated financial statements for the period from January 18, 2018 (inception) to December 31, 2018, material weaknesses were identified in our internal control over financial reporting. A material weakness is a deficiency or combination of deficiencies in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual or interim consolidated financial statements will not be prevented or detected on a timely basis by the company's internal controls. The material weaknesses that were identified related to the following:

- We did not have an internal finance department. Consequently, we lacked sufficient personnel with an appropriate level of knowledge and requisite U.S. generally accepted accounting principles expertise to identify, evaluate and account for complex and non-routine transactions and an adequate supervisory review structure that is needed to comply with financial reporting requirements.
- We did not have an adequate assessment of risks that could significantly impact internal controls over financial reporting and did not effectively design and monitor controls in response to the risks of material misstatement.

In 2019, we implemented plans to remedy these material weaknesses and as of December 31, 2019 our remediation efforts were ongoing. While we believe that these efforts have improved and will continue to improve our internal control over financial reporting, remediation of the material weaknesses will require validation and testing of the design and operating effectiveness of internal controls over a sustained period of financial reporting cycles resulting in the reporting of these material weaknesses as of December 31, 2019. We have implemented and are in the process of implementing additional measures and risk assessment procedures designed to improve our disclosure controls and procedures and internal control over financial reporting to address the underlying causes of these material weaknesses, including the implementation of appropriate segregation of duties, formalization of accounting policies and controls, and implementation of accounting systems to automate manual processes. In 2019, we also hired our Chief Financial Officer, principal accounting officer and additional qualified accounting and finance personnel, formalized our hiring practices, engaged financial consultants to enable the implementation of internal controls over financial reporting and are actively recruiting a new audit committee chair and financial expert (following the resignation of Tomer Kariv, our audit committee chair and financial expert, from our board of directors in December 2019).

We cannot assure you that we have identified all, or that we will not in the future have additional, material weaknesses. Material weaknesses may still exist when we report on the effectiveness of our internal control over financial reporting as required by reporting requirements under Section 404 of the Sarbanes-Oxley Act.

Changes in Internal Control over Financial Reporting

Other than the changes intended to remediate the material weaknesses noted above, no change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) occurred during the quarter ended December 31, 2019 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Management's Annual Report on Internal Control Over Financial Reporting

This Annual Report on Form 10-K does not include a report of management's assessment regarding our internal control over financial reporting (as defined in Rule 13a-15(f) under the Exchange Act) or an attestation report of our independent registered accounting firm due to a transition period established by rules of the Securities and Exchange Commission for newly public companies.

Attestation Report of Registered Public Accounting Firm

As an emerging growth company, we are not required to provide an attestation report on our internal control over financial reporting issued by the Company's independent registered public accounting firm.

Item 9B. Other Information.

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The following table sets forth certain information regarding our executive officers and directors as of March 1, 2020.

Directors and Executive Officers

Name	Age	Position
Executive Officers		
Rohan Palekar	54	Chief Executive Officer and Director
Ram Waisbourd	53	Chief Operating Officer and Chief Business Officer
Ryan Martins	43	Chief Financial Officer
Hank Mansbach, M.D.	55	Chief Medical Officer
Quoc Le-Nguyen	52	Chief Technical Operations Officer and Head of Quality
Non-Employee Directors		
Derek DiRocco, Ph.D.(1)(3)	39	Director
Gregory Grunberg, M.D.(2)(3)	47	Director
Michael Hayden, M.B. Ch.B., Ph.D.(1)(2)	68	Director
Anat Naschitz(2)(3)	52	Director

(1) Member of the Audit Committee
(2) Member of the Compensation Committee
(3) Member of the Nominating and Corporate Governance Committee

Our board of directors is divided into three classes, with members of each class holding office for staggered three-year terms. There are currently two Class I directors (Mr. Palekar and Dr. Grunberg), whose terms expire at the 2020 annual meeting of stockholders; one Class II director (Dr. Hayden), whose term expires at the 2021 annual meeting of stockholders; and two Class III directors (Dr. DiRocco and Ms. Naschitz), whose terms expire at the 2022 annual meeting of stockholders (in all cases until their successors have been elected and qualified or until the earlier of their resignation or removal).

The following is a summary of the experience of our executive officers and directors:

Executive Officers

Rohan Palekar has served as our Chief Executive Officer and a member of our board of directors since June 2018. Prior to joining our company, Mr. Palekar served as the president and Chief Executive Officer of Avanir Pharmaceuticals, Inc., a specialty pharmaceutical company, from December 2015 to July 2017, where he led the company following its acquisition by Otsuka Pharmaceutical Co., Ltd. in 2015. Mr. Palekar also served as Executive Vice President and Chief Operating Officer of Avanir in 2015 and as Senior Vice President and Chief Commercial Officer of Avanir from March 2012 to March 2015. Prior to Avanir, Mr. Palekar served as Chief Commercial Officer for Medivation, Inc., a biopharmaceutical company, from 2008 to 2011, where he was responsible for all commercial activities, chemistry, manufacturing and controls, medical affairs and public relations functions. Prior to Medivation, Mr. Palekar spent over 16 years at Johnson & Johnson, a diversified healthcare company, in various senior commercial and strategic management roles. Mr. Palekar earned his M.B.A. from the Tuck School of Business at Dartmouth College, his B.Com. in Accounting from the University of Mumbai and his L.L.B. in Law from the University of Mumbai.

We believe Mr. Palekar is qualified to serve on our board of directors because of his broad and long experience in the biopharmaceutical industry.

Ram Waisbourd has served as our Chief Operating Officer and Chief Business Officer since May 2018. Prior to joining our company, Mr. Waisbourd served as Vice President of Strategy and Transformation, Global Research and Development, at Teva Pharmaceutical Industries Ltd., a pharmaceutical company, from November 2016 to April 2018, where he was responsible for Teva research and development strategy, novel pipeline funding transactions and digital initiatives. Mr. Waisbourd also served as Vice President of Transformational Initiatives and Operations, Global Research and Development at Teva from September 2015 to October 2016 and Senior Director, Chief of the Research and Development Office from August 2012 to August 2015. Previously, Mr. Waisbourd served as Vice President of Business Development of XTL Biopharmaceuticals Ltd., a biotechnology company, and as Vice President of Biomedical Investments, an investment fund. Mr. Waisbourd earned his M.B.A from Tel-Aviv University and his B.Sc. in Economics from The Wharton School at the University of Pennsylvania.

Ryan Martins has served as our Chief Financial Officer since July 2019 and previously served as our consultant since April 2019. Prior to joining our company, Mr. Martins was Chief Financial Officer at Revolution Medicines, Inc., from March 2018 to October 2018, where he was responsible for all aspects of the finance function including financial accounting, capital planning, audit, tax and investor relations. Before Revolution Medicines, Mr. Martins was Vice President and Head of Corporate Strategy and Investor Relations at Ultragenyx Pharmaceutical, Inc., from September 2015 to March 2018, where he was responsible for strategic planning, capital raising, investor relations and assisting business development. Prior to Ultragenyx, Mr. Martins spent nearly 10 years as a biotechnology analyst at Jefferies, Lazard, and Barclays/Lehman Brothers after holding operating roles at Chiron Corporation from 2001 to 2006. Mr. Martins earned his B.Sc. in Life Sciences from St. Xavier's College, a M.S. degree in Biology from Virginia Tech and an M.B.A. from the Haas School of Business at U.C. Berkeley.

Hank Mansbach, M.D. has served as our Chief Medical Officer since December 2018. Prior to joining our company, Dr. Mansbach was at Ultragenyx Pharmaceutical Inc., a biotechnology company where he served Head of Global Clinical Development for Metabolic and Neurologic Diseases from June 2018 to December 2018, Vice President of Global Clinical Development and Ultra Programs from March 2017 to June 2018 and Vice President of Medical Affairs from May 2015 to March 2017. During his time at Ultragenyx, Dr. Mansbach was responsible for leading clinical development programs for metabolic disorders and building and leading the Medical Affairs team. Before Ultragenyx, Dr. Mansbach served as Vice President of Medical Affairs at Medivation, Inc., a biopharmaceutical company, from August 2009 to April 2015, where he played a key role in the development and commercialization of enzalutamide for the treatment of advanced prostate cancer. Earlier in his career, Dr. Mansbach served as Senior Vice President of Global Drug Development at Valeant Pharmaceuticals and Chief Medical Officer at Cortex Pharmaceuticals, Inc., a pharmaceutical company. Dr. Mansbach began his industry career at Glaxo Wellcome after clinical practice and research in neurology. He earned his M.D. from Duke University and a B.A. in Philosophy from Yale University.

Quoc Le-Nguyen has served as our Chief Technical Operations Officer and Head of Quality since March 2019. Prior to joining our company, Mr. Le-Nguyen was Senior Vice President, Global Head of Technical Operations & Quality for Aduro BioTech, Inc., a biotechnology company, from September 2015 to July 2018, where he was responsible for clinical supply including analytical and process development, manufacturing, supply chain and quality for cell therapy, small molecule and antibody platforms. Prior to Aduro, Mr. Le-Nguyen was the Vice President of Manufacturing Operations for Bayer AG from September 2007 to September 2013, where he was responsible for the Betaferon/Betaseron franchise. Prior to Bayer, Mr. Le-Nguyen worked in biologics manufacturing for Novartis International AG, Chiron Corporation and BioMarin Pharmaceutical Inc. Mr. Le-Nguyen earned his B.S. in Biochemistry from the University of California, Davis.

Non-Employee Directors

Derek DiRocco, Ph.D. has served as a member of our board of directors since April 2018. Dr. DiRocco has been a principal at RA Capital Management, LLC, an investment advisory firm that invests in healthcare and life science companies, since December 2017 and was previously an analyst from June 2015 to December 2017 and an associate from July 2013 to June 2015. Dr. DiRocco earned his Ph.D. in Pharmacology from the University of Washington and his B.A. in Biology from College of the Holy Cross.

We believe Dr. DiRocco is qualified to serve on our board of directors because of his experience as an investor in biotechnology companies and role in early stage companies.

Gregory Grunberg, M.D. has served as a member of our board of directors since April 2018. Dr. Grunberg has been a Managing Director at Longitude Capital Management Co., LLC, a venture capital firm, since February 2012. Prior to joining Longitude, Dr. Grunberg was a Principal at Rho Ventures, a venture capital firm, where he worked from May 2007 to January 2012. Dr. Grunberg maintains a limited clinical practice in internal medicine and affiliations with University of California, San Francisco and Kaiser Permanente. Dr. Grunberg has served on the boards of Kala Pharmaceuticals Inc., a pharmaceutical company, since April 2016, and WelbeHealth LLC, a private healthcare services company, since April 2018. He has served as a board observer at Sydnexis, Inc., a private biotechnology company, since September 2017. He previously served on the board of California Cryobank (acquired by GI Partners) from August 2014 to August 2018 and led Longitude's investment in Practice Fusion (acquired by Allscripts Healthcare Solutions, Inc.). While at Rho Ventures he served on the board of AqueSys Inc. (acquired by Allergan plc) from June 2010 to December 2011 and was a board observer at both SARCode Bioscience Inc. (acquired by Shire plc) from June 2011 to February 2012 and PHT Corporation (acquired by eResearchTechnology, Inc.) from November 2010 to November 2012. Dr. Grunberg earned his M.D. and M.B.A. from Duke University and his A.B. in Economics and English from Amherst College.

We believe Dr. Grunberg is qualified to serve on our board of directors because of his extensive experience investing in and guiding early phase companies.

Michael Hayden, M.B. Ch.B., Ph.D. has served as a member of our board of directors since April 2018. Dr. Hayden has served as a Killam Professor at the University of British Columbia since 1983 and serves as the director of the Translational Laboratory in Genetic Medicine at the National University of Singapore and A*STAR. Dr. Hayden was the President of Global Research and Development and Chief Scientific Officer at Teva Pharmaceutical Industries Ltd., a pharmaceutical company, from May 2012 to December 2017, and served as an advisor to Teva from December 2017 to August 2018. During this time approximately 35 new products were approved in major markets with many for diseases of the CNS such as migraine. He led the development of the first deuterated drug to be approved by the FDA and the second drug ever to be approved for Huntington disease. He is also the Founder and a Senior Scientist of the Centre for Molecular Medicine and Therapeutics at the University of British Columbia. Dr. Hayden has served on the boards of AbCellera Biologics Inc., a biopharmaceutical company, since October 2019, Aurinia Pharmaceuticals Inc., a biopharmaceutical company, since February 2018, Ionis Pharmaceuticals, Inc., a biopharmaceutical company, since September 2018, and Xenon Pharmaceuticals, Inc., a pharmaceutical company, since November 1996. Dr. Hayden received his M.B. Ch.B. in Medicine, Ph.D. in Genetics and Diploma in Child Health from the University of Cape Town. He received his American Board Certification in both internal medicine and clinical genetics from Harvard Medical School and an FRCPC in internal medicine from the University of British Columbia.

We believe Dr. Hayden is qualified to serve on our board of directors because of his extensive experience as a senior executive and member of the board of other life science companies.

Anat Naschitz has served as a member of our board of directors since January 2018, and played a key role in creating 89Bio Ltd. as a spinout from a pharmaceutical company. Ms. Naschitz has served as Managing Director at OrbiMed, a global healthcare investment firm, since January 2010. Ms. Naschitz has over 20 years of healthcare experience. Previously, Ms. Naschitz created, invested in and advised healthcare companies across stages and substance. She was an Associate Partner with McKinsey in London from 1995 to 2002, where she managed strategy, company formation through spinouts and mergers and acquisitions projects for senior management of the world's leading pharmaceutical and biotechnology companies. Subsequently Ms. Naschitz was a Principal at Apax Partners, where she invested in healthcare companies. She currently serves on the boards of biotech and digital health companies and served on the board of Medigus Ltd., a medical device company, from March 2013 to June 2017. Ms. Naschitz earned her M.B.A. at INSEAD and her L.L.B. at Tel Aviv University.

We believe Ms. Naschitz is qualified to serve on our board of directors because of her long industry experience and experience as an investor in biotechnology companies.

Family Relationships

There are no family relationships among any of our directors or executive officers.

Code of Conduct

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. A copy of the code is available on the Corporate Governance section of our website, which is located at *http://ir.89bio.com/corporate-governance/governance-overview*. We intend to disclose on our website any amendments to, or waivers from, the code of business conduct and ethics that are required to be disclosed pursuant to the disclosure requirements of Item 5.05 of Form 8-K within four business days following the date of the amendment or waiver.

Audit Committee and Audit Committee Financial Expert

We have a separately-designated standing audit committee established in accordance with Section 3(a)(58)(A) of the Exchange Act. Dr. DiRocco and Dr. Hayden serve on the audit committee. Our board of directors has determined that each member of the audit committee is "independent" for audit committee purposes as that term is defined in the rules of the SEC and the applicable Nasdaq Listing Rules, and has sufficient knowledge in financial and auditing matters to serve on the audit committee. We do not currently have an audit committee financial expert as defined in Item 407(d)(5) of Regulation S-K promulgated under the Securities Act or audit committee chair following Mr. Kariv's resignation from the board of directors in December 2019. However, our board of directors intends to retain an audit committee financial expert and audit committee chair in the near future.

Item 11. Executive Compensation.

Our named executive officers ("NEOs") for 2019, which consist of our principal executive officer and our two other most highly compensated executive officers who served during the year ended December 31, 2019, are:

- Rohan Palekar, our Chief Executive Officer;
- Hank Mansbach, our Chief Medical Officer; and
- Quoc Le-Nguyen, our Chief Technical Operations Officer and Head of Quality.

Summary Compensation Table

The following table sets forth information regarding compensation earned by our NEOs during the years ended December 31, 2019 and 2018.

Name and Principal Position(1)	Year	Salary ($)	Bonus ($)(2)	Option Awards ($)(3)	All Other Compensation ($)		Total ($)
Rohan Palekar, Chief Executive Officer	2019	430,844	320,000	267,301	4,466	(4)	1,022,611
	2018	194,792	97,396	414,908	1,065		708,161
Hank Mansbach, Chief Medical Officer(5)	2019	380,000	208,993	175,951	—		764,944
Quoc Le-Nguyen, *Chief Technical Operations Officer and Head of Quality*(5)	2019	269,167	102,000	183,487	3,195	(4)	557,849

(1) Mr. Palekar, Dr. Mansbach and Mr. Le-Nguyen commenced employment as of July 16, 2018, December 17, 2018 and March 18, 2019, respectively.
(2) Following the end of the fiscal year, we awarded each NEO a bonus in respect of company and individual performance in fiscal year 2019 and, for Dr. Mansbach $35,000 in respect of his efforts in connection with the completion of our initial public offering.
(3) Amounts shown in this column represent the aggregate grant date fair value (calculated in accordance with FASB Accounting Standards Codification Topic 718) of stock options granted during the year. A description of the methodologies and assumptions we use to value equity awards and the manner in which we recognize the related expense are described in Note 9 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K, Share-Based Compensation. These amounts may not correspond to the actual value eventually realized by each NEO because the value depends on the market value of our common stock at the time the award is exercised.
(4) Represents 401(k) employer matching contribution.
(5) We have omitted Dr. Mansbach's and Mr. Le-Nguyen's compensation for 2018 in accordance with SEC rules as neither was an NEO in that year.

Outstanding Equity Awards at 2019 Fiscal-Year End

The following table sets forth information regarding outstanding equity awards as of December 31, 2019 for each of our NEOs.

	Option Awards				
Name	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable		Option Exercise Price ($)	Option Expiration Date
Rohan Palekar	101,634	223,597	(1)	1.93	11/09/2028
	—	132,242	(2)	3.11	07/30/2029
Hank Mansbach	24,551	73,653	(1)	1.93	01/10/2029
		39,037	(2)	3.11	07/30/2029
Quoc Le-Nguyen	—	65,008	(1)	3.11	07/30/2029
		26,486	(2)	3.11	07/30/2029

(1) Twenty-five percent of the stock option award vests on the one-year anniversary of the employee's start date (July 16, 2018, in the case of Mr. Palekar, December 17, 2018, in the case of Dr. Mansbach and March 18, 2019, in the case of Mr. Le-Nguyen) and the remainder vests in equal quarterly installments thereafter, subject to continued service through each such vesting date.

(2) Twenty-five percent of the stock option award vests on July 23, 2020 and the remainder vests in equal quarterly installments thereafter, subject to continued service through each such vesting date.

Employment Agreements

Mr. Palekar

During 2019, we were party to an offer letter agreement with Mr. Palekar, effective as of July 16, 2018, pursuant to which he serves as our chief executive officer. The agreement provides for a base salary, eligibility to receive an annual performance bonus and eligibility to participate in employee benefit or group insurance plans maintained from time to time by the Company. The agreement also provided for the grant of a stock option award in 2018 as reported in the Summary Compensation Table. The agreement provides for employment on an at-will basis and thus either party may terminate at any time for any or no reason, subject to the severance provisions described below in the section titled "Post-Employment Compensation and Change in Control Payments and Benefits."

Dr. Mansbach

During 2019, we were party to an offer letter agreement with Dr. Mansbach, effective as of December 17, 2018, pursuant to which he serves as our chief medical officer. The agreement provides for a base salary, eligibility to receive an annual performance bonus and eligibility to participate in employee benefit or group insurance plans maintained from time to time by the Company. The agreement also provided for the grant of a stock option award in 2018. The agreement provides for employment on an at-will basis and thus either party may terminate at any time for any or no reason, subject to the severance provisions described below in the section titled "Post-Employment Compensation and Change in Control Payments and Benefits."

Mr. Le-Nguyen

During 2019, we were party to an offer letter agreement with Mr. Le-Nguyen, effective as of March 18, 2019, pursuant to which he serves as our chief technical operations officer. The agreement provides for a base salary, eligibility to receive an annual performance bonus and eligibility to participate in employee benefit or group insurance plans maintained from time to time by the Company. The agreement also provided for the grant of a stock option award in 2019. The agreement provides for employment on an at-will basis and thus either party may terminate at any time for any or no reason, subject to the severance provisions described below in the section titled "Post-Employment Compensation and Change in Control Payments and Benefits."

For 2019, Mr. Palekar's annualized base salary was $425,000, which was increased to $437,750 in July 2019 as part of the annual merit review process, Dr. Mansbach's annualized base salary was $380,000, and Mr. Le-Nguyen's annualized base salary was $340,000.

Incentive Compensation

Annual Incentive. For fiscal year 2019, Mr. Palekar, Dr. Mansbach and Mr. Le-Nguyen had target bonus opportunities equal to 45% of base salary through July 15, 2019 and 50% thereafter, 35% of base salary and 30% of base salary, respectively (subject to proration for any partial-year service).

Following the end of the fiscal year, our board of directors evaluated the performance of Mr. Palekar, Dr. Mansbach and Mr. Le-Nguyen, and based on Company and individual performance in 2019, determined to award bonuses to the named executive officers as disclosed in the Summary Compensation Table above. The board of directors also awarded Dr. Mansbach a $35,000 bonus for his efforts in connection with the completion of our initial public offering.

Equity Incentive. During 2019, all of our named executive officers received stock option awards under our 89Bio Ltd. 2018 Equity Incentive Plan (the "2018 Plan"). In connection with the Reorganization, in September 2019, our board of directors adopted and our stockholders approved our 2019 Equity Incentive Plan (the "2019 Plan"), the successor to the 2018 Plan. All stock awards granted under the 2018 Plan prior to the effective time of the 2019 Plan that were outstanding as of the effectiveness of the 2019 Plan were canceled and replaced with equivalent awards under the 2019 Plan. See the table titled "Outstanding Equity Awards at 2019 Fiscal-Year End" for more information with respect to these grants.

Post-Employment Compensation and Change in Control Payments and Benefits

Severance

Pursuant to the terms of the offer letter agreements with the NEOs, upon a termination without cause (as defined in the agreements) not in connection with a change in control (as defined in the agreements), the NEOs will receive, subject to execution and non-revocation of a release of claims in favor of the Company (the "release condition"), severance equal to six months (in the case of Mr. Palekar), four months (in the case of Dr. Mansbach) or three months (in the case of Mr. Le-Nguyen) of the base salary as then in effect, a pro-rata amount of the target bonus opportunity based on the number of months employed during the year of termination and payment or reimbursement of COBRA premiums for up to six months (in the case of Mr. Palekar), four months (in the case of Dr. Mansbach) or three months (in the case of Mr. Le-Nguyen), or, if sooner, until eligible for similar coverage through another employer.

If the NEO is terminated without cause or for good reason (as defined in the agreements) within 90 days prior to, or 12 months following, the consummation of a change in control, then, subject to the release condition, the benefits described above will be provided for 12 months (in the case of Mr. Palekar) or six months (in the case of the other NEOs) and all outstanding equity awards will vest in full.

401(k) Plan

We offer eligible employees, including our NEOs based in the United States, the opportunity to participate in our tax-qualified 401(k) plan. Employees can contribute 1%-100% of their eligible earnings up to the Internal Revenue Service's annual limits on a before-tax basis. For every dollar an employee contributes up to 6% of their compensation, we may contribute 25 cents per dollar, provided that there are no matching contributions in excess of 1.5% of eligible IRS compensation. Matches provided to our NEOs are reflected in the "All Other Compensation" column of the Summary Compensation Table above. Our funds are 100% vested after the completion of one year of service.

Director Compensation

The following table sets forth the total cash and equity compensation paid to our non-employee directors for service on our board of directors during 2019:

Name	Fees Earned or Paid in Cash ($)(1)	Option Awards ($)(2)	Total ($)
Michael Hayden	40,006	82,764	122,770
Derek DiRocco	—	—	—
Gregory Grunberg	—	—	—
Tomer Kariv	—	—	—
Anat Naschitz	—	—	—

(1) Dr. Hayden is party to a letter agreement with the Company pursuant to which the Company pays him a monthly fee of $3,333 for service on the Board. The fees payable to the non-employee directors for their service on the board of directors from the completion of our initial public offering through the end of the fiscal year have not yet been determined. The Company expects to determine and pay such amounts in the first quarter of fiscal 2020 and will disclose such payments via a Current Report on Form 8-K.

(2) Amounts shown in this column represent the aggregate grant date fair value (calculated in accordance with FASB Accounting Standards Codification Topic 718) of stock options granted during the year. A description of the methodologies and assumptions we use to value equity awards and the manner in which we recognize the related expense are described in Note 9 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K, Share-Based Compensation. These amounts may not correspond to the actual value eventually realized by the director because the value depends on the market value of our common stock at the time the award is exercised. As of December 31, 2019, Dr. Hayden held 134,214 outstanding stock options, of which 36,692 were exercisable. No other non-employee director held any outstanding equity awards as of such date.

We did not compensate Mr. Palekar for his service on our board of directors during 2019 and we do not expect to compensate our employee directors for their service on our board of directors in the future.

Non-Employee Director Compensation Policy

Our board of directors has adopted a non-employee director compensation policy that went into effect following our initial public offering. Under the policy, each director who is not an employee was entitled to receive cash compensation as set forth below:

Annual retainer for board of directors membership	$	40,000
Additional annual retainer for service as a committee chair*	$	10,000
Additional annual retainer for service as chairman of the board of directors	$	60,000

* Applies with respect to each of the audit, compensation and nominating and corporate governance committees.

Following the end of the fiscal year, our board of directors approved the following changes to the non-employee director compensation policy:

Annual retainer for board of directors membership (other than the chair)	$	40,000
Additional annual retainer for service as chair of the audit committee	$	15,000
Additional annual retainer for service as chair of the compensation and governance committees	$	10,000
Additional annual retainer for service as a member of the audit committee	$	7,500
Additional annual retainer for service as a member of the compensation committee	$	5,000
Additional annual retainer for service as a member of the governance committee	$	4,000
Annual retainer for service as chairman of the board of directors	$	70,000

We pay all such amounts in quarterly installments.

In addition, the compensation committee of our board of directors may in its discretion grant equity awards to any or all non-employee directors under the 2019 Plan. Such awards may include: (i) an initial, one-time equity award granted to a new non-employee director upon his or her election to our board of directors; (ii) equity awards granted to non-employee directors on an annual basis for their service on our board of directors; and/or (iii) equity awards granted to non-employee directors on an annual basis for their service in a leadership role or on a committee of our board of directors. During 2019, prior to our initial public offering, we awarded Dr. Hayden, our sole independent director, 9,380 stock options that vested 25% on April 16, 2019 with the remainder vesting in equal quarterly installments thereafter and 36,367 stock options that will vest 25% on July 23, 2020 with the remainder vesting in equal quarterly installments thereafter.

We reimburse all necessary and reasonable out-of-pocket expenses incurred by non-employee directors in connection with their service on our board of directors, subject to any applicable Company policies that may be in effect from time to time.

A non-employee director may decline all or any portion of his or her compensation by giving notice to us prior to, as the case may be, the date cash is to be paid or equity awards are to be granted.

Our board of directors periodically reviews our director compensation program and may revise the compensation arrangements for our directors from time to time.

Compensation Committee Interlocks and Insider Participation

None of the members of our compensation committee has at any time during the prior three years been one of our officers or employees. None of our executive officers currently serves, or in the past fiscal year has served, as a member of our board of directors or compensation committee of any entity that has one or more executive officers serving on our board of directors or compensation committee.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

Security Ownership of Certain Beneficial Owners and Management

The following table presents information regarding beneficial ownership of our equity interests as of March 1, 2020 by:

- each stockholder or group of stockholders known by us to be the beneficial owner of more than 5% of our outstanding equity interests (our "5% and Greater Stockholders");
- each of our directors;
- each of our NEOs; and
- all of our current directors and executive officers as a group.

Beneficial ownership is determined in accordance with the rules of the SEC, and thus represents voting or investment power with respect to our securities. Under such rules, beneficial ownership includes any shares over which the individual has sole or shared voting power or investment power as well as any shares that the individual has the right to acquire within 60 days after the date of this table to our knowledge and subject to applicable community property rules, the persons and entities named in the table have sole voting and sole investment power with respect to all equity interests beneficially owned.

The percentage ownership information shown in the column titled “Percentage of Shares Beneficially Owned” in the table below is based on 13,788,982 shares of our common stock outstanding as of the date of this table. Unless otherwise indicated, the address of each individual listed in this table is 142 Sansome Street, Second Floor, San Francisco, CA 94104.

Name and Address of Beneficial Owner	Number of Shares Beneficially Owned	Percentage of Shares Beneficially Owned
5% and Greater Stockholders		
Entities affiliated with OrbiMed(1)	4,004,422	29.0 %
Longitude Venture Partners III, L.P.(2)	2,491,787	18.1 %
Entitles affiliated with RA Capital(3)	3,161,214	22.9 %
Entities affiliated with Pontifax(4)	1,134,671	8.2 %
Entities affiliated with Venrock(5)	1,000,000	7.3 %
Named Executive Officers and Directors		
Rohan Palekar(6)	142,288	1.0 %
Hank Mansbach(7)	30,688	*
Quoc Le-Nguyen(8)	16,252	*
Derek DiRocco	—	*
Gregory Grunberg(2)	2,491,787	18.1 %
Michael Hayden(9)	126,650	*
Anat Naschitz	—	*
All Executive Officers and Directors as a group (9 persons)	2,868,816	20.8 %

* Represents beneficial ownership of less than one percent.

(1) Based on a Schedule 13D filed on November 25, 2019. Consists of (a) 2,002,221 shares of common stock owned by OrbiMed Israel Partners II, L.P. and (b) 2,002,221 shares of common stock owned by OrbiMed Private Investments VI, L.P. The business address of OrbiMed Israel Partners II, L.P. (“OIP II”) is 89 Medinat Hayehudim St., building E, Herzliya 4614001 Israel. OrbiMed Israel GP II, L.P. (“Israel GP II”) is the general partner of OIP II, and OrbiMed Advisors Israel II Limited (“Advisors Israel II”) is the general partner of Israel GP II. Advisors Israel II and Israel GP II may be deemed to have shared voting and investment power over all of the shares of common and convertible preferred stock held by OIP II, and both Advisors Israel II and Israel GP II may be deemed to directly or indirectly, including by reason of their mutual affiliation, to be the beneficial owners of the shares held by OIP II. Advisors Israel II exercises this investment power through an investment committee comprised of Carl L. Gordon, Jonathan T. Silverstein, Nissim Darvish, Anat Naschitz, and Erez Chimovits, each of whom disclaims beneficial ownership of the shares held by OIP II.

(2) Based on a Schedule 13D filed on November 11, 2019. Longitude Capital Partners III, LLC (“LCP III”) is the general partner of Longitude Venture Partners III, L.P. (“LVP III”) and may be deemed to have shared voting, investment and dispositive power over the shares held by LVP III. Patrick G. Enright and Juliet Tammenoms Bakker are managing members of LCP III and in their capacity as such, may be deemed to exercise shared voting and investment power over the shares held by LCP III and LVP III. Gregory Grunberg is a member of LCP III. Each of these individuals disclaims beneficial ownership of such shares except to the extent of his or her pecuniary interest therein. Gregory Grunberg shares in the control of the Company securities held directly or indirectly by LVP III/LCP III due to (a) his beneficial ownership in the Company’s shares and (b) his position as a director of the Company. The mailing address of Longitude Venture Partners III, L.P. is 2740 Sand Hill Road, 2nd Floor, Menlo Park, CA 94025.

(3) Based on a Schedule 13D filed on November 13, 2019. Consists of (a) 2,342,954 shares of common stock owned by RA Capital Healthcare Fund, L.P. (“RA Capital Fund”), (b) 482,896 shares of common stock owned by a separately managed account (the “Account”), and (c) 335,364 shares of common stock owned by RA Capital Nexus Fund, L.P. (the “RA Capital Nexus Fund”). Dr. Peter Kolchinsky is the managing member of RA Capital Management, LLC (“RA Capital”), the general partner and investment advisor of RA Capital Fund and the investment advisor of the Account and RA Capital Nexus Fund. Dr. Kolchinsky and RA Capital may be deemed to beneficially own the shares held by RA Capital Fund, the Account and RA Capital Nexus Fund. Dr. Kolchinsky and RA Capital disclaim beneficial ownership of all applicable shares except to the extent of their actual pecuniary interest therein. The mailing address for the entities listed above is 200 Berkeley Street, 18th Floor, Boston, MA 02116.

(4) Based on a Schedule 13G filed on February 14, 2020. Consists of (a) 668,732 shares of common stock owned by Pontifax (Israel) V, L.P., (b) 178,623 shares of common stock owned by Pontifax (Cayman) V, L.P., (c) 259,816 shares of common stock owned by Pontifax (China) V, L.P. (together, the “Pontifax Entities”), and (d) 27,500 shares of common stock owned by Pontifax Late Stage Fund L.P. (“Late Stage L.P.”). Pontifax 5 G.P. L.P. (“Pontifax 5 G.P.”) is the general partner of each of the Pontifax Entities and Pontifax Management 4 G.P. (2015) Ltd. (“Pontifax Management”) is the general partner of Pontifax 5 G.P. Mr. Tomer Kariv and Mr. Ran Nussbaum, are the Managing Partners of Pontifax Management and, as a result, may be deemed to share voting and investment power with respect to the shares held by each of the Pontifax Entities. Late Stage L.P. invests side by side with Pontifax 5 GP pursuant to a Strategic Alliance Agreement with Pontifax 5 GP. Pontifax Late Stage GP Ltd. is the general partner of Late Stage L.P. The address of each of the Pontifax Entities and Late Stage L.P. is c/o The Pontifax Group, 14 Shenkar Street, Herzelia, Israel.

(5) Based on a Schedule 13G filed on November 25, 2019. Consists of (a) 29,339 shares of common stock owned by Venrock Healthcare Capital Partners II, L.P. ("VHCP II LP"), (b) 11,896 shares of common stock owned by VHCP Co-Investment Holdings II, LLC ("VHCP Co-Investment II"), (c) 871,613 shares of common stock owned by Venrock Healthcare Capital Partners III, L.P. ("VHCP III LP"), and (d) 87,152 shares of common stock owned by VHCP Co-Investment Holdings III, LLC ("VHCP Co-Investment III"). VHCP Management II, LLC ("VHCP Management II") is the general partner of VHCP II LP and the manager of VHCP Co-Investment II. VHCP Management III, LLC ("VHCP Management III" and collectively with VHCP II LP, VHCP Co-Investment II, VHCP III LP, VHCP Co-Investment III and VHCP Management II, the "Venrock Entities") is the general partner of VHCP III LP and the manager of VHCP Co-Investment III. Nimish Shah and Bong Koh are the voting members of VHCP Management II and VHCP Management III. The address of each of the Venrock Entities and Messrs. Shah and Koh is 7 Bryant Park, 23rd Floor, New York, NY 10018.
(6) Consists of 142,288 shares of common stock underlying options that are exercisable as of March 1, 2020 or will become exercisable within 60 days after such date.
(7) Consists of 30,688 shares of common stock underlying options that are exercisable as of March 1, 2020 or will become exercisable within 60 days after such date.
(8) Consists of 16,252 shares of common stock underlying options that are exercisable as of March 1, 2020 or will become exercisable within 60 days after such date.
(9) Consists of (a) 77,728 shares of common stock owned by Genworks 2 Consulting Inc., over which Dr. Hayden's wife has sole voting and investment power, and (b) 48,922 shares of common stock underlying options that are exercisable as of March 1, 2020 or will become exercisable within 60 days after such date. The address of Genworks 2 Consulting Inc. is 4484 West 7th Avenue, Vancouver, BC, Canada V6R1W9.

Securities Authorized for Issuance Under Equity Compensation Plans

The following table contains information about our equity compensation plans as of December 31, 2019. As of December 31, 2019, we had two equity compensation plans: our Amended and Restated 2019 Equity Incentive Plan ("2018 Plan") and our 2019 Employee Stock Purchase Plan ("2019 ESPP").

Equity Compensation Plan Information

Plan Category	Number of securities to be issued upon exercise of outstanding options, warrants and rights (a)	Weighted average exercise price of outstanding options, warrants and rights (b)	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a)) (c)	
Equity compensation plans approved by security holders	1,320,243	$ 3.34	1,749,138	(1) (2)
Equity compensation plans not approved by security holders	—	—	—	
Total	1,320,243	$ 3.34	1,749,138	

(1) Includes 1,523,950 shares available for grant under the 2019 Equity Incentive Plan.
(2) Includes 225,188 shares available for grant under the 2019 Employee Stock Purchase Plan.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

The following is a summary of each transaction or series of similar transactions since January 18, 2018, our inception, to which we were a party in which:

- the amount involved exceeds $120,000 or one percent of the average of the our total assets at year end for the last two completed fiscal years; and
- any of our directors or executive officers or any beneficial owners of 5% of any class of our voting capital stock or and affiliate or immediate family member thereof, had or will have a direct or indirect material interest, other than compensation and other arrangements that are described under the section titled "Executive Compensation" or that were approved by our compensation committee.

Beneficial ownership is determined in accordance with the rules of the SEC and generally includes voting or investment power with respect to such securities.

Related Party Transactions

In April 2018, with subsequent closings in December 2018 and June and July 2019, we issued an aggregate of 44,000,000 shares of our Series A convertible preferred shares at a purchase price of $1.00 per share pursuant to a share purchase agreement entered into with investors, for an aggregate purchase price of approximately $44.0 million. Each share of our Series A convertible preferred shares automatically converted into 0.161 shares of our common stock immediately prior to the completion of our initial public offering ("IPO") in November 2019. Additionally, in April 2018, we issued 610,865 shares of our common stock shares to OrbiMed Israel Partners II, L.P. and OrbiMed Private Investments VI, L.P., for total proceeds of $10,994. The following table summarizes purchases of our Series A convertible preferred shares by related persons:

Participant	Shares of Series A Convertible Preferred Shares	Total Purchase Price
Entities affiliated with OrbiMed(1)	15,888,888	$ 15,888,888
Entities affiliated with Pontifax(2)	5,500,001	$ 5,500,001
Entities affiliated with RA Capital(3)	10,327,777	$ 10,327,777
Longitude Venture Partners III, L.P.(4)	11,916,667	$ 11,916,667
Genworks 2 Consulting Inc.(5)	366,667	$ 366,667

(1) OrbiMed Israel Partners II, L.P. ("OrbiMed Israel") together with its affiliate fund OrbiMed Private Investments VI, L.P. is a holder of 5% or more of our capital stock. Anat Naschitz is a managing director at OrbiMed Israel and a member of our board of directors.
(2) Pontifax (Israel) V L.P., together with its affiliate funds Pontifax (Cayman) V L.P. and Pontifax (China) V L.P., is a holder of 5% or more of our capital stock. Tomer Kariv is co-founder and managing partner of the Pontifax Group and was a member of our board of directors until December 2019.
(3) RA Capital Healthcare Fund, L.P. together with its affiliate funds Blackwell Partners LLC - Series A and RA Capital Nexus Fund, L.P. is a holder of 5% or more of our capital stock. Derek DiRocco is a principal at RA Capital Management, LLC and a member of our board of directors.
(4) Longitude Venture Partners III, L.P. is a holder of 5% or more of our capital stock. Gregory Grunberg, M.D. is a Managing Director at Longitude Capital Management Co., LLC and a member of our board of directors.
(5) Dr. Michael Hayden, a member of our board of directors, is affiliated with Genworks 2 Consulting Inc.

In November 2019, we closed our IPO of 6,100,390 shares of common stock at a public offering price of $16.00 per share. The net proceeds were $87.7 million after deducting underwriting discounts and commissions and offering costs. In the IPO, entities affiliated with OrbiMed purchased 837,500 shares of common stock through the underwriters at the IPO price for an aggregate purchase price of $13.4 million. Entities affiliated with Pontifax purchased 250,000 shares of common stock through the underwriters at the IPO price for an aggregate purchase price of $4.0 million. Entities affiliated with RA Capital purchased 1,500,000 shares of common stock through the underwriters at the IPO price for an aggregate purchase price of $24.0 million. Longitude Venture Partners III, L.P. purchased 575,000 shares of common stock through the underwriters at the IPO price for an aggregate purchase price of $9.2 million. Genworks 2 Consulting Inc. purchased 18,750 shares of common stock through the underwriters at the IPO price for an aggregate purchase price of $0.3 million.

We are a party to an investors' rights agreement, effective as of September 17, 2019 (the "IRA"), with our stockholders who previously held our Series A convertible preferred shares, including our 5% stockholders and entities affiliated with our directors. The IRA provides these holders the right to demand that we file a registration statement or request that their shares be covered by a registration statement that we are otherwise filing.

We are party to a voting agreement, effective as of September 17, 2019 (the "Voting Agreement"), with our stockholders who previously held our Series A convertible preferred shares, including our 5% stockholders and entities affiliated with our directors. Each of our 5% stockholders has appointed representatives to our board of directors. The voting agreement terminated upon completion of our IPO, and members previously elected to our board of directors pursuant to this agreement will continue to serve as directors until they resign, are removed or their successors are duly elected by the holders of our common stock.

We are a party to a right of first refusal and co-sale agreement, effective as of September 17, 2019 (the "ROFR Agreement"), with our stockholders who previously held our Series A convertible preferred shares, including our 5% stockholders and entities affiliated with our directors. The ROFR Agreement terminated upon completion our IPO.

Other than the above described sales of securities, the IRA, the Voting Agreement, the ROFR Agreement and the compensation arrangements for our named executive officers and directors, which are described elsewhere in the "Executive and Director Compensation" sections of this Annual Report on Form 10-K, we have not been a party to any transaction since January 18, 2018, our inception, in which the amounts involved exceeded or will exceed the lesser of $120,000 or one percent of the average of our total assets at year end for the last two years, and any of our directors, executive officers or holders of more than 5% of our capital stock, or any member of the immediate family of, or person sharing the household with, the foregoing persons, had or will have a direct or indirect material interest.[1]

Board Determination of Independence

Rule 5605 of the Nasdaq Listing Rules requires a majority of a listed company's board of directors to be comprised of independent directors within one year of listing. In addition, the Nasdaq Listing Rules require that, subject to specified exceptions, each member of a listed company's audit, compensation and nominating and corporate governance committees be independent under the Securities Exchange Act of 1934, as amended (the "Exchange Act"). Audit committee members must also satisfy the independence criteria set forth in Rule 10A-3 under the Exchange Act, and compensation committee members must also satisfy the independence criteria set forth in Rule 10C-1 under the Exchange Act. Under Rule 5605(a)(2) of the Nasdaq Listing Rules, a director will only qualify as an "independent director" if, in the opinion of our board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In order to be considered independent for purposes of Rule 10A-3, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors, or any other board committee, accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries or otherwise be an affiliated person of the listed company or any of its subsidiaries. In order to be considered independent for purposes of Rule 10C-1, the board must consider, for each member of a compensation committee of a listed company, all factors specifically relevant to determining whether a director has a relationship to such company which is material to that director's ability to be independent from management in connection with the duties of a compensation committee member, including, but not limited to: (1) the source of compensation of the director, including any consulting advisory or other compensatory fee paid by such company to the director; and (2) whether the director is affiliated with the company or any of its subsidiaries or affiliates.

Our board of directors undertook a review of the composition of our board of directors and its committees and the independence of each director. Based upon information requested from and provided by each director concerning his or her background, employment and affiliations, including family relationships, our board of directors has determined that each of our current directors listed above under the "Directors and Executive Officers" section of this Annual Report on Form 10-K (as well as Tomer Kariv, who served as a director until December 2019), with the exceptions of Rohan Palekar, is an "independent director" as defined under Rule 5605(a)(2) of the Nasdaq Listing Rules (or was independent during the time of service on our board). Mr. Palekar is not an independent director under Rule 5605(a)(2) because he is our chief executive officer.

Our board of directors also determined that each of the directors currently serving on the audit committee (Dr. DiRocco and Dr. Hayden) satisfy the independence standards for audit committees established by the SEC and the Nasdaq Listing Rules, including the independence requirements contemplated by Rule 10A-3 under the Exchange Act. In addition, our board of directors determined that each of the directors currently serving on the compensation committee (Dr. Grunberg, Dr. Hayden and Ms. Naschitz) satisfy the independence standards for compensation committees established by the SEC and the Nasdaq Listing Rules, including the independence requirements contemplated by Rule 10C-1 under the Exchange Act. In making such determinations, our board of directors considered the relationships that each such non-employee director has with our company and all other facts and circumstances our board of directors deemed relevant in determining independence, including the beneficial ownership of our capital stock by each non-employee director.

1 **Note to Draft:** To be confirmed via D&O questionnaire updates that no additional transactions need to be disclosed.

Item 14. Principal Accounting Fees and Services.

Audit Fees and Services

Deloitte & Touche LLP is our independent registered public accounting firm for the year ended December 31, 2019. Brightman Almagor Zohar & Co., a Firm in the Deloitte Global Network, was our independent registered public accounting firm for the year ended December 31, 2018. The following table summarizes the fees of Deloitte & Touche LLP (after December 24, 2019) and Brightman Almagor Zohar & Co., a Firm in the Deloitte Global Network (before December 24, 2019) billed to us for each of the last two fiscal years. All of such services and fees were pre-approved by our audit committee in accordance with the "Pre-Approval Policies and Procedures" described below.

Fee Category	2019	2018
Audit Fees(1)	$ 496,387	$ 30,590
Audit-Related Fees	—	—
Tax Fees(2)	120,549	18,425
All Other Fees	—	—
Total Fees	$ 616,936	$ 49,015

(1) "Audit Fees" consist of fees for the audit of our annual financial statements, reviews of quarterly financial statements included in Quarterly Reports on Forms 10-Q, and services provided in connection with SEC filings, including consents and comment and comfort letters.

(2) "Tax Fees" consist of fees for services for tax compliance, tax advice, and tax planning.

Pre-Approval Policies and Procedures

Our audit committee has adopted procedures requiring the pre-approval of all audit and non-audit services performed by our independent registered public accounting firm in order to assure that these services do not impair the auditor's independence. These procedures generally approve the performance of specific services subject to a cost limit for all such services. This general approval is to be reviewed, and if necessary modified, at least annually. Management must obtain the specific prior approval of the audit committee for each engagement of the independent registered public accounting firm to perform other audit-related or other non-audit services. The audit committee does not delegate its responsibility to approve services performed by the independent registered public accounting firm to any member of management. Our audit committee has delegated authority to the committee chair to pre-approve any audit or non-audit service to be provided to us by our independent registered public accounting firm provided that the fees for such services do not exceed $100,000. Any approval of services by the committee chair pursuant to this delegated authority must be reported to the audit committee at the next meeting of the committee.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

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

(1) Financial Statements

See Index to Consolidated Financial Statements at Part II, Item 8 "Financial Statements and Supplementary Data."

(2) Financial Statement Schedules

The financial statement schedules are omitted as they are either not applicable or the information required is presented in the financial statements and notes thereto under Part II, Item 8. "Financial Statements and Supplementary Data."

(3) Exhibits:

Exhibit Index

Exhibit Number	Description
2.1	Contribution and Exchange Agreement, dated as of September 17, 2019, by and among 89Bio Ltd., the Company and its shareholders (filed with the SEC as Exhibit 2.1 to the Company's Form S-1 filed on October 11, 2019)
3.1	Second Amended and Restated Certificate of Incorporation of the Company (filed with the SEC as Exhibit 3.1 to the Company's Form 8-K filed on November 15, 2019)
3.2	Second Amended and Restated Bylaws of the Company (filed with the SEC as Exhibit 3.2 to the Company's Form 8-K filed on November 15, 2019)
4.1	Specimen common stock certificate of the Company (filed with the SEC as Exhibit 4.1 to the Company's Form S-1/A filed on October 28, 2019)
4.2	Investors' Rights Agreement, dated as of September 17, 2019, by and among the Company and certain of its shareholders (filed with the SEC as Exhibit 4.2 to the Company's Form S-1 filed on October 11, 2019)
4.3*	Description of Securities
10.1+	Form of Indemnification Agreement for directors and executive officers (filed with the SEC as Exhibit 10.1 to the Company's Form S-1 filed on October 11, 2019)
10.2+	Amended and Restated 2019 Equity Incentive Plan and form of agreements thereunder (filed with the SEC as Exhibit 10.2 to the Company's Form S-1/A filed on October 28, 2019)
10.3+	2019 Employee Stock Purchase Plan (filed with the SEC as Exhibit 10.3 to the Company's Form S-1/A filed on October 28, 2019)
10.4+	Executive Employment Offer Letter, dated June 25, 2018, by and between 89Bio Ltd. and Rohan Palekar (filed with the SEC as Exhibit 10.4 to the Company's Form S-1 filed on October 11, 2019)
10.5+	Executive Employment Agreement, dated April 23, 2018, by and between 89Bio Ltd. and Ram Waisbourd (filed with the SEC as Exhibit 10.5 to the Company's Form S-1 filed on October 11, 2019)
10.6+	Executive Employment Offer Letter, dated November 20, 2018, by and between 89Bio Ltd. and Hank Mansbach (filed with the SEC as Exhibit 10.6 to the Company's Form S-1 filed on October 11, 2019)
10.7+	Executive Employment Offer Letter, dated February 28, 2019, by and between 89Bio Ltd. and Quoc Le-Nguyen (filed with the SEC as Exhibit 10.7 to the Company's Form S-1 filed on October 11, 2019)
10.8+	Executive Employment Offer Letter, dated July 21, 2019, by and between 89Bio Ltd. and Ryan Martins (filed with the SEC as Exhibit 10.8 to the Company's Form S-1 filed on October 11, 2019)
10.9+	Director Offer Letter, dated July 1, 2018, by and between 89Bio Ltd. and Michael Hayden (filed with the SEC as Exhibit 10.9 to the Company's Form S-1 filed on October 11, 2019)
10.10+	Non-Employee Director Compensation Policy (filed with the SEC as Exhibit 10.10 to the Company's Form S-1/A filed on October 28, 2019)
10.11†	Asset Transfer and License Agreement—FGF21 by and among 89Bio Ltd., ratiopharm GmbH, Teva Branded Pharmaceutical Products R&D, Inc. and Teva Pharmaceutical Industries Ltd, dated as of April 16, 2018 (filed with the SEC as Exhibit 10.11 to the Company's Form S-1 filed on October 11, 2019)
10.12+	Reagent Supply and Technology Transfer Agreement by and between 89Bio Ltd. and Teva Biotech GmbH, dated as of April 16, 2018, as amended (filed with the SEC as Exhibit 10.12 to the Company's Form S-1 filed on October 11, 2019)

Exhibit Number	Description
10.13+	Sublicense Agreement by and between 89Bio Ltd. and ratiopharm GmbH, dated as of April 16, 2018 (filed with the SEC as Exhibit 10.13 to the Company's Form S-1 filed on October 11, 2019)
10.14+	Master Services Agreement by and between 89Bio Ltd. and Biotechpharma UAB, dated as of May 7, 2018, as amended (filed with the SEC as Exhibit 10.14 to the Company's Form S-1 filed on October 11, 2019)
10.15*	Office Lease by and between 89bio, Inc. and King Family Irrevocable Trust, dated as of December 5, 2019.
16.1	Letter from Brightman Almagor Zohar & Co., dated December 31, 2019 (filed with the SEC as Exhibit 16.1 to the Company's Current Report on Form 8-K filed on December 31, 2019).
21.1+	List of subsidiaries (filed with the SEC as Exhibit 21.1 to the Company's Form S-1 filed on October 11, 2019)
23.1*	Consent of Independent Registered Public Accounting Firm
23.2*	Consent of Independent Registered Public Accounting Firm
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934.
31.2*	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934.
32.1#	Certification of Principal Executive Officer and Principal Financial Officer Pursuant to 18 U.S.C. Section 1350.
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Label Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

* Filed herewith.

\+ Indicates management contract or compensatory plan.

† Portions of the exhibit have been omitted for confidentiality purposes.

\# Furnished herewith and not deemed to be "filed" for purposes of Section 18 of the Exchange Act, and shall not be deemed to be incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act.

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, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized**.**

89bio, Inc.

Date: March 18, 2020 By: /s/ Rohan Palekar

Rohan Palekar
Chief Executive Officer and Director
(principal executive officer)

Date: March 18, 2020 By: /s/ Ryan Martins

Ryan Martins
Chief Financial Officer
(principal financial and accounting officer)

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below hereby constitutes and appoints Rohan Palekar, Ram Waisbourd and Ryan Martins, and each of them, the true and lawful attorneys-in-fact and agents of the undersigned, with full power of substitution and resubstitution, for and in the name, place and stead of the undersigned, to sign in any and all capacities (including, without limitation, the capacities listed below), this Annual Report on Form 10-K, any and all amendments thereto, and to file the same, with all exhibits thereto, and all other documents in connection therewith, with the Securities and Exchange Commission, and hereby grants to such attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and anything necessary to be done to enable the registrant to comply with the provisions of the Securities Exchange Act and all the requirements of the Securities and Exchange Commission, as fully to all intents and purposes as the undersigned might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or any of them, or their or 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 in the capacities and on the dates indicated.

Name	Title	Date
/s/ Rohan Palekar **Rohan Palekar**	Chief Executive Officer and Director (*principal executive officer*)	March 18, 2020
/s/ Ryan Martins **Ryan Martins**	Chief Financial Officer (*principal financial and accounting officer*)	March 18, 2020
/s/ Derek DiRocco **Derek DiRocco, Ph.D.**	Director	March 18, 2020
/s/ Gregory Grunberg **Gregory Grunberg, M.D.**	Director	March 18, 2020
/s/ Michael Hayden **Michael Hayden, M.B., Ch.B., Ph.D.**	Director	March 18, 2020
/s/ Anat Naschitz **Anat Naschitz**	Director	March 18, 2020

Exhibit 4.3

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

The following description of our capital stock is intended as a summary only and therefore is not a complete description of our capital stock. This description is based upon, and is qualified by reference to, our second amended and restated certificate of incorporation (the "Amended Certificate"), our second amended and restated bylaws (the "Amended Bylaws") and applicable provisions of Delaware corporate law. You should read our Amended Certificate and Amended Bylaws, which are filed as exhibits to our Annual Report on Form 10-K, to which this exhibit is also appended.

Our authorized capital stock consists of 100,000,000 shares of common stock and 10,000,000 shares of preferred stock.

Common Stock

Our Amended Certificate authorizes the issuance of up to 100,000,000 shares of our common stock. All outstanding shares of our common stock are validly issued, fully paid and nonassessable.

The holders of our common stock are entitled to one vote per share on all matters submitted to a vote of stockholders. A majority vote of the shares present in person or represented by proxy and entitled to vote on the subject matter is required for the holders of our common stock to take action on all matters (except for election of directors (as discussed below)), except as otherwise required by law, our Amended Certificate or our Amended Bylaws. Our Amended Certificate does not provide for cumulative voting in the election of directors. The holders of our common stock will receive ratably any dividends declared by our board of directors out of funds legally available therefor. In the event of our liquidation, dissolution or winding-up, the holders of our common stock will be entitled to share ratably in all assets remaining after payment of or provision for any liabilities.

Preferred Stock

Under the terms of our Amended Certificate, 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, to establish from time to time the number of shares to be included in each such series, to fix the dividend, voting and other rights, preferences and privileges of the shares of each wholly unissued series and any qualifications, limitations or restrictions thereon, and to increase or decrease the number of shares of any such series, but not below the number of shares of such series then outstanding.

Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of our common stock. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring or preventing a change in our control and may adversely affect the market price of our common stock and the voting and other rights of the holders of our common stock.

Registration Rights

The holders of 7,077,366 shares of our common stock are entitled to rights with respect to the registration of these securities under the Securities Act of 1933, as amended (the "Securities Act"). These rights are provided under the terms of our investors' rights agreement, effective as of September 17, 2019 (the "IRA"). The IRA includes demand registration rights, short-form registration rights and piggyback registration rights. All fees, costs and expenses of underwritten registrations under this agreement will be borne by us and all selling expenses, including underwriting discounts and selling commissions, will be borne by the holders of the shares being registered.

Demand Registration Rights

Beginning on May 6, 2020, the holders of 7,077,366 shares of our common stock are entitled to demand registration rights. Under the terms of the IRA, we will be required, upon the written request of at least 50% of the holders of the registrable securities, including either OrbiMed Israel Partners II, L.P. or OrbiMed Private Investments VI, LP, provided that the anticipated aggregate offering price is at least $10 million, to file a registration statement on Form S-1 and use commercially reasonable efforts to effect the registration of these shares for public resale. The right to have such shares registered on Form S-1 is further subject to other specified conditions and limitations.

Piggyback Registration Rights

Pursuant to the IRA, if we register any of our common stock either for our own account or for the account of other security holders, the holders of registrable shares party to the IRA are entitled to include their shares in the registration, subject to certain marketing and other limitations. We may terminate or withdraw any registration initiated before the effective date of such registration in our sole discretion.

Form S-3 Registration Rights

Pursuant to the IRA, if we are eligible to file a registration statement on Form S-3, upon the written request of at least 10% of the holders of registrable securities to sell registrable securities at an aggregate price of at least $5 million, we will be required to use commercially reasonable efforts to effect a registration of such shares. The right to have such shares registered on Form S-3 is further subject to other specified conditions and limitations.

Anti-Takeover Effects of Our Amended Certificate, Amended Bylaws and Delaware Law

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

- ***Issuance of undesignated preferred stock:*** Under our Amended Certificate, 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 Certificate establishes 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 of directors.
- ***Election and removal of directors and board vacancies:*** Our Amended Bylaws provide that directors will be elected by a plurality vote. Our Amended Certificate and Amended Bylaws also provide that our board of directors has the right to increase or decrease the size of the board and to fill vacancies on the board. Directors may be removed only for cause by the affirmative vote of the holders of at least 66⅔% of the votes that all our stockholders would be entitled to cast in an annual election of directors. Only our board of directors is authorized 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 the directors then in office. These provisions prevent stockholders 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.

- ***Requirements for advance notification of stockholder nominations and proposals:*** Our Amended Bylaws establish advance notice procedures with respect to stockholder proposals and the nomination of candidates for election as directors that specify certain requirements as to the timing, form and content of a stockholder's notice. Business that may be conducted at an annual meeting of stockholders will be limited to those matters properly brought before the meeting. 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.
- ***No written consent of stockholders:*** Our Amended Certificate provides that all stockholder actions be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting. This limit may lengthen the amount of time required to take stockholder actions and would prevent the amendment of our Amended Bylaws or removal of directors by our stockholders without holding a meeting of stockholders**.**
- ***No stockholder ability to call special meetings:*** Our Amended Certificate and Amended Bylaws provide that only a majority of the members of our board of directors then in office may be able to call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders.
- ***Amendments to certificate of incorporation and bylaws:*** Any amendment to our Amended Certificate will be required to be approved by a majority of our board of directors as well as, if required by law or the Amended Certificate, a majority of the outstanding shares entitled to vote on the amendment and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of provisions to board classification, stockholder action, certificate amendments, and liability of directors must be approved by not less than 66⅔% of the outstanding shares entitled to vote on the amendment, voting together as a single class. Any amendment to our Amended Bylaws must be approved by either a majority of our board of directors or not less than 66⅔% of the outstanding shares entitled to vote on the amendment, voting together as a single class.

These provisions are designed 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 the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner.

Choice of Forum

Our Amended Certificate requires that the Court of Chancery of the State of Delaware be the exclusive forum for the following types of actions or proceedings under Delaware statutory or common law: (1) any derivative action or proceeding brought on our behalf; (2) any action asserting a breach of fiduciary duty owed by any director, officer or other employee to us or our stockholders; (3) 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 Certificate or Amended Bylaws; or (4) 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 Securities Exchange Act of 1934, as amended, or any other claim for which the federal courts have exclusive jurisdiction. Our Amended Certificate 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. Although we believe these provisions benefit us by providing increased consistency in the application of Delaware law for the specified types of actions and proceedings, the provisions may have the effect of discouraging lawsuits against us or our directors or officers.

Transfer Agent and Registrar

American Stock Transfer and Trust Company, LLC serves as the transfer agent and registrar for our common stock.

Listing

Our common stock is listed on The Nasdaq Global Market under the symbol “ETNB.”

142 SANSOME STREET

Office Lease

Between

KING FAMILY
IRREVOCABLE TRUST

AS LANDLORD

AND

89bio, Inc.

AS TENANT

TABLE OF CONTENTS

Basic Lease Information

142 Sansome Street

The following is a summary of *Basic Lease Information*. To the extent there is any conflict between the provisions of this Summary and any provision of the Lease, the Lease provision shall control.

LEASE DATE:	December 5, 2019
LANDLORD:	KING FAMILY IRREVOCABLE TRUST
ADDRESS OF LANDLORD:	c/o King & Co. Investment Management Inc. 142 Sansome Street, Suite 600 San Francisco, CA 94104
TENANT:	89bio, Inc.
ADDRESS OF TENANT:	142 Sansome Street, 2nd Floor San Francisco, CA 94104
PREMISES:	Floor: 2nd; Rentable Square Footage: 3,554 142 Sansome Street San Francisco, CA 94104
LEASE TERM:	Two (2) Years
RENEWAL OPTION:	One (1) Two (2) Years Option to Renew
BASE RENT:	OFFICE SPACE BASE RENT Year 1: $59.00 psf, per annum fully serviced or $17,473.83 per month Year 2: $60.77 psf, per annum fully serviced or $17,998.05 per month
SCHEDULE COMMENCEMENT DATE:	January 15, 2020
RENT COMMENCEMENT DATE:	January 15, 2020
EXPIRATION DATE:	January 14, 2020
BASE EXPENSE YEAR:	2020
USE:	General Office Use
TENANT'S PERCENTAGE SHARE:	18.79%
INITIAL SECURITY DEPOSIT:	$71,992.20
TENANT'S BROKER:	T3 Advisors 140 Geary St, Ste 1000 San Francisco, CA 94108 Attn: Andrew Zink / Allison Hoffman

LANDLORD'S BROKER:	Kidder Mathews 101 Mission St, Suite 1800 San Francisco, CA 94105 Attn: Brad Van Blois
ATTACHMENTS:	Exhibit A - Rules and Regulations Exhibit B - Floor Plan Exhibit C - Tenant's Work Exhibit D - Disability Access Obligations Under SF Administrative Code Chapter 38 Exhibit E - SF Small Business Commission's Access Information Notice

OFFICE LEASE

PARTIES

1. This Lease is made this 5th day of December, 2019 between King Family Irrevocable Trust, as Landlord, and 89bio, Inc. as Tenant,

WITNESSETH:

PREMISES

2. Landlord hereby leases to Tenant and Tenant hereby hires from Landlord those certain premises (hereinafter called "premises") being the entire 2nd floor of that certain building (hereinafter called "building") known as 142 Sansome Street, San Francisco, CA, 94104.

   Said letting and hiring is upon and subject to the terms, covenants and conditions herein set forth and Tenant covenants as a material part of the consideration for this Lease to keep and perform each and all of said terms, covenants and conditions by it to be kept and performed and that this Lease is made upon the condition of such performance.

PURPOSE

3. The premises shall be used for general office purposes and for no other use or purpose without the prior written consent of Landlord.

TERM

4. The term of this Lease shall be for two (2) years, commencing on the 15th day of January, 2020, and ending on the 14th day of January, 2022 (the "Lease Term"). Landlord shall provide Tenant access to the premises between December 9, 2019 to December 19, 2019 without any obligation to pay rent for the sole purpose of Tenant's work (see Exhibit C). In addition, beginning January 6, 2020 Tenant shall have access to complete Tenant's Work and for installation of furniture, fixtures and equipment. No access to the premises will be given to Tenant during December 20, 2019 to January 5, 2020.

4.1 Option to Extend

Tenant shall have the option to extend the Lease Term for an additional period of two (2) years (the "Extension Term"). The Extension Term shall be on all the terms and conditions of this Lease, except that Tenant shall not have the option to further extend the Lease Term and the rental rate will be at Market Value (as defined in Paragraph 6(c)). Tenant must exercise its option to extend the Lease Term by written notice to Landlord no less than one hundred eighty (180) days and no more than two hundred seventy (270) days prior to the end of the initial "Lease Term."

POSSESSION

5. If Landlord, for any reason whatsoever, cannot deliver possession of the premises to Tenant at the commencement of the term hereof, this Lease shall not be void or voidable, nor shall Landlord be liable to Tenant for any loss or damage resulting therefrom, but in that event there shall be a proportionate reduction of rent covering the period between the commencement of the term and the time when Landlord can deliver possession. Should Landlord tender possession of the premises to Tenant prior to the date specified for the commencement of the term, and Tenant accepts such prior tender, such prior occupancy shall be subject to all terms, covenants, and conditions of this Lease. No delay in delivery of possession shall operate to extend the term hereof. Tenant hereby accepts the premises in its "AS IS" condition with the exception that Tenant, at Tenant's sole cost and expense shall perform the work to the premises which is identified on Exhibit C attached hereto. The premises will be delivered vacant, broom clean, with all furniture and personal property removed and all building systems in good operating condition.

RENT

6. (a) On or before the first day of each calendar month during the term hereof Tenant shall pay to Landlord, as minimum monthly rent for the premises, the sum described in the *Basic Lease Information*. The minimum monthly rent for any partial month (inclusive of the month of February) shall be prorated at the rate of 1/30 of the minimum monthly rent per day. Notwithstanding the foregoing, Tenant shall pay to Landlord together with Tenant's execution of this Lease, an amount equal to the monthly base rent payable for the first full calendar month of the Lease term, which amount shall be applied to the monthly base rent first due and payable hereunder.

Said rent shall be paid by Tenant to Landlord, c/o King & Co. Investment Management Inc., in advance, without deduction or offset, in lawful money of the United States of America at King & Co. Investment Management Inc., 142 Sansome Street, Suite 600, San Francisco, California, 94104 or to such other person or to such other place as Landlord may from time to time designate in writing.

(b) All charges and other amounts of any kind payable by Tenant to Landlord pursuant to this Lease shall be deemed additional rent. Landlord shall have the same remedies for default in the payment of additional rent as for default in the payment of basic rent. Basic rent and additional rent are collectively sometimes hereinafter referred to as rent.

(c) If Tenant exercises its option to extend the Lease Term pursuant to Paragraph 4.1, the monthly rent payable during such extension period shall be adjusted as of the first (1st) day of the extension term (the "Market Rent Date") to the Market Rent, determined as follows:

Definition. The term "Market Rent" shall mean the monthly amount per rentable square foot in the Premises that a willing, non-equity, non-renewal, non-expansion new tenant would pay and a willing landlord would accept at arm's length for space in a comparable building or buildings, with comparable tenant improvements, in a comparable location, giving appropriate consideration to monthly rental rates per rentable square foot, the presence or absence of periodic rent escalations, operating expenses and tax pass-throughs, length of lease term, site and location of premises being leased, and other generally applicable terms and conditions of tenancy for a similar building or buildings; provided, however, Market Rent shall in no event be less than the minimum monthly rent during the last month of the initial Lease term.

Agreement on Market Rent. No later than one hundred eighty (180) days prior to the Market Rent Date, Landlord and Tenant, upon notice from Landlord, shall agree on the Market Rent. If the parties are unable to agree on the Market Rent, the parties shall choose a licensed Real Estate Appraiser who shall determine the Market Rent. The cost of said Real Estate Appraiser shall be borne equally by the parties. If the parties are unable to agree on a licensed Real Estate Appraiser, each party shall select one Appraiser to appraise the Market Rent. If the difference between the two appraisals is 20% or less of the lower appraisal, then the Market Rent shall be the average of the two appraisals. If the difference between the two appraisals is greater than 20% of the lower appraisal, the two Appraisers shall select a third licensed Real Estate Appraiser to appraise the Market Rent. The Market Rent shall in such case be the average of the three appraisals. The cost of the third appraisal shall be borne equally by the parties.

Amendment of Lease. Immediately after the Market Rent is determined pursuant to this Paragraph 6(c), Landlord and Tenant shall execute an amendment to the Lease stating the new Base Rent in effect.

RENTAL ADJUSTMENT

7. (a) In addition to the monthly rent provided for in Paragraph 6 hereof, Tenant shall pay to Landlord the sums set forth in the following subparagraphs. Tenant's percentage share as set forth below has been calculated by dividing the number of square feet of rentable area in the Premises by the number of square feet of rentable area in the building. In the event the rentable area of the building is changed, the Tenant's percentage share shall be appropriately adjusted. Rentable area shall be based upon the then current Building Owners and Managers Association International (BOMAI) standard method of floor measurement for office buildings. Tenant hereby approves and accepts Landlord's calculation of Tenant's current percentage share as set forth below.

(b) Tax Increases and Assessments

Tenant shall pay to Landlord Tenant's percentage share of any increase in real property taxes and assessments or other fees or charges of whatsoever kind or character imposed by a governmental agency which may be levied on the land and building of which the premises are a part and personal property taxes levied on personal property of Landlord used in the operation of said land and building above the amount of such taxes levied and assessed for the Base Tax Year, either by way of increase in the rate or in the assessed valuation of said land and building or by imposition of any such charges by ordinance or statute of any authority having jurisdiction. For the purposes of the foregoing, (a) real and personal property taxes shall include, without limitation, taxes of every kind and nature levied and assessed in lieu of or in substitution for existing or additional real or personal property taxes on said land and building as well as any form of assessment, license, fee, levy, penalty, or tax (other than income, inheritance or estate taxes), imposed by any authority having the direct or indirect power to tax, including any city, county, state, or federal government, or any school, agriculture, lighting, drainage, or other improvement district, as against any legal or equitable interest of Landlord in the premises or in the real property of which the premises are a part, or as against Landlord's right to rent or other income therefrom, or as against Landlord's business of leasing

the premises. In addition, Tenant shall pay one hundred per cent (100%) of any increase in taxes or assessments of whatsoever kind and nature (including, without limitation, all personal property taxes) caused by improvements or installations made by Tenant to the premises at any time during the term hereof. The total amounts due hereunder shall be paid to Landlord on or before the date full payment of such taxes or assessments or, if payable in installments, the date payment of the first installment of such taxes or assessments shall become due. In the event said taxes or assessments are charged to or paid or payable by Landlord, Tenant forthwith upon demand therefore, shall reimburse Landlord for all amounts of such taxes or assessments chargeable against Tenant pursuant to this subparagraph (b) and paid by Landlord.

(c) Operating Expense Increases

Tenant shall pay to Landlord, at the times hereinafter set forth, an amount equal to Tenant's percentage share of any increase in direct expenses paid or incurred by Landlord on account of the operation or maintenance of the building above such direct expenses paid or incurred by Landlord during the Base Expense Year. "Direct Expenses" as used herein shall include all direct costs of operation and maintenance as determined by standard accounting practices as set forth in the Building Owners and Managers Association International (BOMAI) chart of accounts from time to time (excluding, however, any and all taxes of the nature set forth in subparagraph (b) above) and shall include the following by way of illustration but not limitation: the cost of contesting by appropriate proceeding the amount or the validity of any of the aforementioned taxes or fees; water and sewer charges; insurance premiums, license; permit and inspection fees; charges for all power; janitorial services; labor; supplies; materials, equipment and tools; management expenses and the cost of capital improvements made by Landlord to the building that are intended to reduce other Operating Expenses or that are required under any governmental law or regulation that is not applicable to the building as of the date of this Lease, such cost or allocable portion thereof to be amortized over such reasonable period as Landlord shall determine together with interest on the unamortized balance at the rate that was paid by Landlord on funds borrowed for the purpose of constructing or installing such capital improvements, or, if Landlord does not borrow such funds, would have been paid had the Landlord borrowed funds for such purpose but in no event shall such interest rate exceed the maximum rate permitted by law. "Direct expenses" as used herein shall not include depreciation on the building, real estate broker's commissions, tenant improvements, interest and capital items other than those referred to above.

Statements of the amount of direct expenses for the preceding calendar year and the amount of such increase payable by Tenant shall be determined or estimated by Landlord and shall be given to Tenant on such date as Landlord shall from time to time determine. All amounts payable by Tenant as shown on said statement shall be paid by Tenant within the time required by said statement. If during any such year Landlord shall revise its estimate of Tenant's share of said expense for said year, Landlord shall advise Tenant and commencing on the next date payment of additional charges are due, Tenant shall pay all additional charges based on such revised estimate for the portion of the year already elapsed and shall commence paying the additional charges based on such revised estimate for the remainder of such year.

SECURITY DEPOSIT

8. Simultaneously with the execution of this Lease, Tenant shall deposit with Landlord the sum of $71,992.20 which shall be held by Landlord as security for the faithful performance by Tenant of all the terms, covenants and conditions of this Lease. Provided that at the end of the term Tenant shall have delivered up the Premises to Landlord, broom clean, and in the same condition as at the commencement date, reasonable wear excepted, said sum held as security shall be returned to Tenant. No interest shall be payable thereon and Landlord shall not be required to keep said sum in a separate account. If Tenant fails to pay any Rent or other charges due hereunder, or otherwise defaults with respect to any provision of this Lease, Landlord may at its option apply or retain all or any portion of the deposit for the payment of any Rent or other charge in default or the payment of any other sum to which Landlord may become obligated by Tenant's default, or to compensate Landlord for any loss or damage which Landlord may suffer thereby. If Landlord so uses or applies all or any portion of the deposit, then within 10 days after demand therefor Tenant shall deposit cash with Landlord in an amount sufficient to restore the deposit to the full amount thereof, and Tenant's failure to do so shall be a material breach of this Lease. Landlord's application or retention of the deposit shall not constitute a waiver of Tenant's default to the extent that the deposit does not fully compensate Landlord for all losses or damages incurred by Landlord in connection with such default and shall not prejudice any other rights or remedies available to Landlord under this Lease or by law. Tenant hereby unconditionally and irrevocably waives the benefits and protections of California Civil Code Section 1950.7, and, without limitation of the scope of such waiver, acknowledges that Landlord may use all or any part of the security deposit to compensate Landlord for damages resulting from termination of this Lease and the tenancy created hereunder (including, without limitation, damages recoverable under California Civil Code Section 1951.2).

   No security or guaranty which may now or hereafter be furnished Landlord for the payment of the rent herein reserved or for performance by Tenant of the other covenants or conditions of this Lease shall in any way be a bar or defense to any action in unlawful detainer, or for the recovery of the premises, or to any action which Landlord may at any time commence for a breach of any of the covenants or conditions of this Lease.

LATE CHARGE

9. All rent payable by Tenant to Landlord hereunder, if not received by Landlord within five (5) days after its due date, shall bear a late charge equal to ten percent (10%) of the amount due together with interest accruing from the date due at the maximum interest rate permitted by law, which late charge and interest shall be payable forthwith upon demand. (The foregoing shall be in addition to any other right or remedy of Landlord.)

USES PROHIBITED

10. Tenant shall not do or permit anything to be done in or about the premises nor bring or keep anything therein which will in any way increase the rate of or affect any fire or other insurance upon the building or any of its contents or cause a cancellation of any insurance policy covering said building or contents. Tenant shall not do or permit anything to be done in or about the

premises which will in any way obstruct or interfere with the rights of other Tenants or occupants of the building or injure or annoy them, or use or allow the premises to be used for any residential, immoral, unlawful or objectionable purpose, nor shall Tenant cause, maintain or permit any nuisance in, on or about the premises. No cooking devices or other odor causing devices, water filtration devices or dispensers, dishwashers, loudspeakers or other similar device, system or apparatus which can be heard or experienced outside the premises shall, without the prior written approval of Landlord, be used in or at the premises. Tenant shall not commit or suffer to be committed any waste in or upon the premises.

COMPLIANCE WITH LAW

11. Tenant shall not use or permit anything to be done in or about the premises which will in any way conflict with any law, statute, ordinance or governmental rule, regulation or requirement now in force or which may hereafter be enacted or promulgated. Tenant, at its sole cost and expense, shall promptly comply with all laws, statutes, ordinances and governmental rules, regulations or requirements now in force or which may hereafter be in force and with the requirements of any board of fire underwriters or other similar body now or hereafter constituted relating to or affecting the condition, use of occupancy of the premises, excluding structural changes not related to or affected by Tenant's improvements or acts. The judgement of any court of competent jurisdiction or the admission of Tenant in an action against Tenant, whether Landlord be a party thereto or not, that Tenant has violated any law, statute, ordinance or governmental rule, regulation or requirement shall be conclusive of that fact as between Landlord and Tenant. Further, Tenant shall at all times and in all respects comply with all federal, state and local laws, ordinances and regulations ("Hazardous Materials Laws") relating to hygiene, environmental protection, or the presence, use generation, storage, transportation or disposal of any toxic or hazardous substances, as the same may be amended from time to time, including without limitation, obtaining any required permits or licenses, and Tenant shall handle, treat, manage and dispose of any and all toxic or hazardous substances in strict conformity with all manufacturers' instructions and prudent business practices.

ALTERATIONS

12. Tenant shall not make or suffer to be made any alterations, additions or improvements to or of the premises or any part thereof without the written consent of Landlord first had and obtained. Any alterations, additions or improvements to or of said premises, including without limitation any partitions, movable or otherwise, and all carpeting, shall at once become a part of the realty and belong to Landlord. Movable furniture, equipment and trade fixtures shall remain the property of Tenant. If Landlord consents to the making of any alterations, additions or improvements to the premises by Tenant, the same shall be made by Tenant at Tenant's sole cost and expense and any contractor or person selected by Tenant to make the same must first be approved of in writing by Landlord. Upon the expiration or sooner termination of the term Tenant, upon demand by Landlord, at Tenant's sole cost and expense, forthwith and with all due diligence shall remove any alterations, additions or improvements made by Tenant designated by Landlord to be removed, and Tenant, forthwith and with all due diligence, at its sole cost and expense, shall repair any damage to the premises caused by such removal. Tenant's obligation to remove any alterations, additions, improvements, fixtures and/or personal property and to repair any damage from such removal shall survive the termination of this Lease.

Construction of the alterations, additions or improvements shall be completed in accordance with drawings and specifications approved in advance in writing by Landlord, shall be carried out in a good and workmanlike manner, and shall comply with all applicable requirements of governmental authorities and such additional conditions as Landlord may reasonably impose.

Tenant hereby agrees to use reasonable efforts to notify Landlord if Tenant makes any alterations or improvements to the Premises that might impact accessibility to the Premises or Building under any disability access laws, and any disability access improvements to the Building or Premises required due to alterations or improvements made to the Premises by Tenant shall be the responsibility of Tenant. Landlord hereby agrees to use reasonable efforts to notify Tenant if Landlord makes any alterations or improvements to the Premises that might impact accessibility to the Premises or Building under any disability access laws.

REPAIR

13. By entry hereunder upon the commencement of the term hereof, Tenant accepts the premises as being in good, sanitary order, condition and repair. Tenant, at Tenant's sole cost and expense, shall keep the premises and every part thereof in good condition and repair, damage thereto by fire, earthquake, act of God or the elements not caused by Tenant's negligent or willful act excepted, Tenant hereby waiving all rights to make repairs at the expense of the Landlord as provided by law, stature or ordinance now or hereafter in effect, including, without limitation, the provisions of California Civil Code Sections 1932(1), 1941 and 1942. Upon the expiration or sooner termination of the term hereof, Tenant shall surrender the premises to Landlord in the same condition as when received, ordinary wear and tear and damage by fire, earthquake, act of God or the elements excepted, unless caused by Tenant's negligent or willful act. It is specifically understood and agreed that Landlord has no obligation and has made no promises to alter, remodel, improve, repair, decorate or paint the premises or any part thereof and that no representations respecting the condition of the premises or the building have been made by Landlord to Tenant. There shall be no abatement of Rent and no liability to Landlord by reason of any injury or to interference with Tenant's business arising from the making of any repairs or performance of any maintenance obligations by the Landlord. Landlord shall be responsible for maintenance, repairs and replacement, as necessary, of structured elements, building systems and common areas.

ABANDONMENT

14. Tenant shall not vacate or abandon the premises at any time during the term hereof, and if Tenant shall abandon, vacate or surrender the premises or be dispossessed by process of law, or otherwise, any personal property belonging to Tenant and left on the premises shall be deemed to be abandoned, at the option of Landlord.

LIENS

15. Tenant shall keep the premises and the building and the land upon which the building is situated free from any liens arising out of any work performed, materials furnished or obligations incurred by Tenant. Tenant shall in the event of the filing of any such lien, post any bond required to release the premises therefrom. Should Tenant fail to remove any such lien within five (5) business days after notice to do so from Landlord, Landlord may, in addition to any other remedies, record a bond pursuant to California Civil Code Section 3143 and all amounts incurred by Landlord in so doing shall become immediately due and payable by Tenant to Landlord as additional rent. Landlord shall have the right to post and keep posted on the Premises any notices that may be provided by law or which Landlord may deem to be proper for the protection of Landlord, the Premises and the building from such liens.

ASSIGNMENT AND SUBLETTING

16. (a) Tenant shall not mortgage, pledge, hypothecate or encumber this Lease or any interest therein. Tenant shall not assign this Lease or sublet or suffer any other person (the agents and servants of Tenant excepted) to occupy or use the premises, or any part thereof, or sublet any right or privilege appurtenant thereto without the prior written consent of Landlord first had and obtained, which consent shall not be unreasonably withheld. Landlord's consent to one assignment, subleasing or occupancy shall not be deemed to be a consent to any subsequent assignment, subleasing or occupancy.

(b) Provided further and notwithstanding anything herein before set forth: In the event that at any time or from time to time during the term of this Lease, Tenant desires to assign this Lease or sublet all or any part of the Premises, Tenant shall notify the Landlord in writing (the "Transfer Notice") of the terms of the proposed assignment or subletting, and, in the case of a sublease, the area so proposed to be sublet and shall give Landlord the right to (x) terminate this Lease or (y) sublet from Tenant such space proposed to be subleased on the same terms as those contained in the Sublet Notice. Such option shall be exercisable by Landlord in writing for a period of 15 days after receipt of the Sublet Notice.

If Landlord fails to exercise its option and Tenant desires to complete the proposed sublease, Tenant shall deliver an executed copy of such sublease to Landlord in order to obtain its consent as required in paragraph 16(a) above. If Landlord consents to a sublease, then such sublease shall be subject to and made upon the following terms:

(i) any such sublease shall be subject to the terms of this Lease and the term thereof may not extend beyond the expiration of the term of this Lease; and

(ii) no subtenant shall have a right to further sublease its premises.

If Landlord fails to exercise such option, and Tenant fails to consummate a sublease with a third party within 60 days after the expiration of Landlord's option period on the same terms and conditions contained in the Sublet Notice, Tenant shall be required to deliver a new Sublet Notice to Landlord and comply with the terms and conditions set forth above before any further subletting shall be permitted.

(c) Any rent or other consideration realized by Tenant under any assignment or sublease, in excess of the rent and all other amounts (including without limitation, Tenant's share of the increases) payable hereunder (or the amount thereof proportionate to the portion of the premises subject to such sublease or assignment) and reasonable commissions and the cost of any alterations incurred in connection with such sublease or assignment, shall be divided and paid fifty percent (50%) to Landlord and fifty percent (50%) to Tenant.

(d) Regardless of Landlord's consent, no subletting nor assignment shall release Tenant of Tenant's obligation or alter the primary liability of Tenant to pay rent and perform other obligations of Tenant under this Lease.

(e) Tenant shall pay Landlord's reasonable cost, including without limitation of any legal fees, which incurred in connection with Tenant's request to assign this Lease or sublet the premises, regardless whether or not the Landlord consents to the proposed transfer.

(f) If Tenant is a corporation or a partnership, the transfer (as a consequence of a single transaction) of fifty percent (50%) or more of the beneficial ownership interest of the voting stock of Tenant issued and outstanding as of the date hereof or of the partnership interests in Tenant, as the case may be, shall constitute an assignment hereunder for which such consent is required. Any such sublease or assignment without the written consent of Landlord shall be void, and, at the option of Landlord, shall terminate this Lease.

(g) Tenant will have the right in the event of a merger, consolidation, reorganization, or recapitalization, whether or not Tenant survives as the surviving corporation, to assign or transfer this Lease to such surviving corporation; provided, however, such right of assignment or transfer will be limited to an assignee (i) whose net worth is equal to or greater than the net worth of Tenant at the time of such assignment or transfer and (ii) whose historical profitability (in both duration and amount) is equal to or greater than Tenant, as viewed at the time of the proposed assignment or transfer. In the event Tenant contemplates making an assignment or transfer as provided in this subparagraph, Tenant will give thirty (30) days' notice to Landlord of its intention to make such assignment or transfer and will furnish Landlord with all pertinent information as to the net worth of the proposed assignee or transferee.

INDEMNIFICATION OF LANDLORD

17. Tenant agrees to indemnify and defend Landlord against and save Landlord harmless from any and all loss, cost, liability, damage and expense, including without limitation penalties, fines and reasonable attorneys' fees and costs, incurred in connection with or arising from any cause whatsoever in, on or about the premises, including without limiting the generality of the foregoing: (1) any default by Tenant in the observance or performance of any of the terms, covenants or conditions of this Lease on Tenant's part to be observed or performed, or (2) the use of occupancy or manner of the use or occupancy of the premises by Tenant or any other person or entity claiming through or under Tenant, including without limitation, the presence, use, generation, storage, transportation or disposal of any toxic or hazardous substances, or (3) the condition of the premises or any occurrence or happening on the premises from any cause whatsoever, or (4) any acts, omissions or negligence of Tenant or of Tenant's agents, contractors, employees, subtenants, licensees, invitees or visitors or any such person or entity, in, on or about the premises or the building, either prior to the commencement of, during, or after the expiration of the term, including without limitation any acts, omissions or negligence in the making or performing of any alterations. Tenant further agrees to indemnify, defend and save harmless Landlord and Landlord's agents from and against any and all loss, cost, liability, damage and expense, incurred in connection with or arising from any claims by any persons by reason of injury to persons or damage to property occasioned by any use, occupancy condition, occurrence, happening, act, omission or negligence referred to in the preceding sentence. In the event any action or proceeding is brought against Landlord for any claim against which Tenant is obligated to indemnify Landlord hereunder, Tenant upon notice from Landlord shall defend such action or proceeding at Tenant's sole expense by counsel approved by Landlord, which approval shall not be unreasonably withheld. The provisions of this Paragraph 17 shall survive the expiration or earlier termination of this lease.

INSURANCE

18. Tenant agrees to keep in force during the term hereof, at Tenant's expense, (i) public liability and property damage insurance with combined single limits in the amount of not less than $2 million ($2,000,000.00), (ii) employer's liability for bodily injury by disease per person and bodily injury by accident with minimum limits of $1 million ($1,000,000), and (iii) statutory workers' compensation, (iv) an "all risk" or "special causes of loss" property policy in the amount of the full replacement cost covering Tenant's personal property and any alterations made by or at the request of Tenant, with Landlord insured as its interest may appear, and (v) an "all risk" or "special causes of loss" policy of business interruption and/or loss of income insurance covering a period of one (1) year. Said public liability policy shall name Landlord as an additional insured, and shall insure Landlord's contingent liability as respects acts or omissions of Tenant, shall be issued by an insurance company licensed to do business in the state of California; and shall provide that said insurance shall not be cancelled or amended unless thirty (30) days prior written notice to Landlord is first given. Said policy or a certificate thereof shall be delivered to Landlord by Tenant prior to the commencement of the term and each renewal of such insurance. Tenant hereby waives all rights of subrogation against Landlord to which any insurance carrier may at any time become entitled under any policy of insurance carried by Tenant. Landlord herby waives all rights of subrogation against Tenant to which any insurance carrier may at any time become entitled under any policy of insurance carried by Landlord.

UTILITIES

19. Landlord shall furnish to the premises, during the period from 8:00 a.m. to 5:00 p.m., Monday through Friday, except for New Year's Day, Washington's Birthday, Memorial Day, Independence Day, Labor Day, Thanksgiving, Christmas, and other such holidays as are generally recognized in San Francisco, California, and subject to rules and regulations from time to time established by Landlord: (a) heating, air conditioning in amounts required in Landlord's reasonable judgement, for the normal use and occupancy of the Premises, (b) passenger elevator service, (c) electricity, (d) water for lavatory purposes and (e) janitorial services consistent with office buildings in the San Francisco financial district suitable for the use of the premises. It is understood that such passenger elevator service, electricity and water will be available twenty-four (24) hours a day, 365 days a year, subject to force majeure or security procedures. At Tenant's written request, lighting, heating and air conditioning ("HVAC") will be available at hours other than those specified above after twenty-four (24) hour written notice to Landlord (provided that if Tenant fails to provide such written notice 24 hours in advance, Landlord shall nonetheless use good faith efforts to provide such service) and upon Tenant's agreement to pay Landlord's charges for such services. The current charge for such non-standard HVAC is fifty-five dollars ($55) per hour per floor. Tenant understands and agrees that such costs are those currently charged by Landlord as of the date of this Lease, and that such figures are not intended in any way be binding upon Landlord. Landlord shall not be liable for, and Tenant shall not be entitled to any abatement or reduction of rent by reason of Landlord's failure to furnish any of the foregoing when such failure or delay is caused by accident, breakage, repairs, strikes, lockouts or other labor disturbances or labor disputes of any character, or is caused directly or indirectly by the limitation, curtailment, rationing or restrictions on use of water, electricity, gas or any other form of energy serving the premises or the building, or by any other cause, similar or dissimilar. Landlord shall not be liable under any circumstances for loss of business or injury to property, however occurring, through or in connection with or incidental to failure to furnish any of the foregoing. Tenant shall pay and provide for all services and utilities not furnished by Landlord. In no event, however, shall Landlord be liable to Tenant for any loss or damage, including the theft of Tenant's property arising out of or in connection with the failure of any security services, personnel or equipment.

Tenant will not, without the written consent of Landlord, use any apparatus or device in the premises which will in any way increase the amount of electricity, cooling capacity or water usually furnished or supplied for use of the premises for general office purposes or connect with electric current, except through existing electrical outlets in the premises, or water pipes, any apparatus or device for the purpose of using electric current or water. If Tenant shall require water or electric current in excess of that customarily furnished or supplied to other Tenants of the building for use of their premises for general office purposes, Tenant shall first procure the consent of Landlord, which Landlord may refuse, to the use thereof.

PERSONAL PROPERTY AND OTHER TAXES

20. Tenant shall pay, before delinquency, (a) any and all taxes levied or assessed and which become payable during the term hereof upon Tenant's equipment, furniture, fixtures and other personal property located in the premises; (b) any and all taxes or increases therein levied or assessed on Landlord or Tenant by virtue of alterations, additions or improvements to the premises made by Tenant or Landlord at Tenant's request; and (c) any and all taxes payable by Landlord (other than net income taxes) whether or not now customary or within the contemplation of the parties hereto which are upon or measured by the monthly rent or other charges payable hereunder, including, without limitation, any gross receipts tax or excise tax levied by the City and County of San Francisco, the State of California, the Federal government or any other governmental body with respect to the receipt of such rental. In the event said taxes are charged to or paid or payable by Landlord, Tenant, forthwith upon demand therefore, shall reimburse Landlord for all of such taxes paid by Landlord.

RULES AND REGULATIONS

21. Tenant shall faithfully observe and comply with the rules and regulations printed on or annexed to this Lease and all modifications of and additions thereto applicable to all Tenants of the building from time to time put into effect by Landlord of which Tenant shall have notice. Landlord shall not be responsible to Tenant for the nonperformance by any other Tenant or occupant of the building of any of said rules and regulations. However, Landlord shall enforce its rules and regulations in a non-discriminatory manner.

HOLDING OVER

22. If Tenant holds possession of the premises after the term of this lease, Tenant shall, (at option of Landlord to be exercised by Landlord's giving written notice to Tenant and not otherwise) become a Tenant from month to month upon the terms and conditions herein specified, so far as applicable, at a monthly rental equal to one hundred fifty percent (150%) of the office base rent then being paid, payable in advance, in lawful money, and shall continue to be such Tenant until thirty (30) days after Tenant shall have given to Landlord or Landlord shall have given to Tenant a written notice of intent to terminate such monthly tenancy. Unless Landlord shall exercise the option hereby given him, Tenant shall be a Tenant at sufferance only, whether or not Landlord shall accept any rent from Tenant while Tenant is so holding over. In addition, if the Premises are not timely surrendered at the expiration or sooner termination of this Lease, Tenant hereby agrees to indemnify Landlord against all loss or liability resulting from any delay by Tenant in so surrendering the Premises, including, but not limited to, any claims made by any succeeding tenant, losses to Landlord due to lost opportunities to lease to succeeding tenants, and actual attorneys' fees and costs.

SUBORDINATION

23. This Lease shall be subject and subordinate at all times to all ground or underlying leases which may now exist or hereafter be executed affecting the building and/or the land upon which the building is situated and to the lien of any mortgages or deeds of trust in any amount or amounts whatsoever now or hereafter placed on or against said building and/or land or on or against the Landlord's interest or estate therein or on or against any ground or underlying lease without the necessity of having further instruments on the part of Tenant to effectuate such subordination. Notwithstanding the foregoing, Tenant covenants and agrees to execute and deliver, upon demand, such further instruments evidencing such subordination of this Lease to such ground or underlying leases and to the lien of any such mortgages or deeds of trust as may be required by Landlord. Tenant hereby irrevocably appoints Landlord the attorney in fact of Tenant to execute and deliver any such instrument or instruments for or in the name of Tenant. In the event of termination of any ground or underlying lease, or in the event of foreclosure or exercise of any power of sale under any mortgage or deed of trust superior to this Lease or to which this Lease is subject or subordinate, upon Tenant's attornment to the Lessor under such ground or underlying lease or to the purchaser at any foreclosure sale or sale pursuant to the exercise of any power of sale under any mortgage or deed of trust, this Lease shall not terminate and Tenant shall automatically be and become the Tenant of said Lessor under such ground or underlying Lease or to said purchaser, whichever shall make demand therefore.

ENTRY BY LANDLORD

24. Landlord reserves and shall at any and all reasonable times, upon reasonable prior notice to Tenant, except in cases of an emergency, have the right to enter the premises to inspect the same, to supply janitor service and any other service to be provided by Landlord to Tenant hereunder, to submit the premises to prospective purchasers or Tenants, to post notices of non-responsibility, and to alter, improve or repair the premises and any portion of the building without abatement of rent and may for that purpose erect scaffolding and other necessary structures where reasonably required by the character of the work to be performed, always providing the entrance to the premises shall not be blocked thereby and further providing that the business of Tenant shall not be interfered with unreasonably. Tenant hereby waives any claim for damages for any injury or inconvenience to or interference with Tenant's business, any loss of occupancy of quiet enjoyment of the premises, and other loss occasioned by such entry. For each of the aforesaid purposes, Landlord shall at all times have and retain a key with which to unlock all of the doors, in, upon and about the premises excluding Tenant's vaults and safes, and Landlord shall have the right to use any and all means which Landlord may deem proper to open said doors in an emergency in order to obtain entry to the premises, and any entry to the premises obtained by Landlord by any of said means, or otherwise, shall not under any circumstances be construed or deemed to be a forcible or unlawful entry into or a detainer of the premises or an eviction of Tenant from the premises or any portion thereof.

INSOLVENCY OR BANKRUPTCY

25. Either (a) the appointment of a receiver to take possession of all or substantially all of the assets of Tenant, (b) an assignment by Tenant for the benefit of creditors, or (c) any action taken or suffered by Tenant under any insolvency, bankruptcy or reorganization act shall constitute a breach of this Lease by Tenant. Upon the happening of any such event this Lease shall terminate five (5) days after written notice of termination from Landlord to Tenant. In no event shall this Lease be assigned or assignable by reason of any voluntary or involuntary bankruptcy proceedings nor shall any rights or privileges hereunder be an asset of Tenant in any bankruptcy, insolvency or reorganization proceedings.

DEFAULT

26. In the event of any breach or default of Lease by Tenant, which remains uncured after three (3) business days' notice from Landlord to Tenant, or any non-monetary breach or default which remains uncured after fifteen (15) days' notice from Landlord to Tenant, then Landlord, besides any other rights and remedies of Landlord at law or equity, shall have the right either to terminate Tenant's right to possession of the premises and thereby terminate this Lease or to have this Lease continue in full force and effect with Tenant at all times having the right to possession of the premises. Any property of Tenant removed may be stored in a public warehouse or elsewhere at the cost and for the account of Tenant. Upon such termination Landlord, in addition to any other rights and remedies (including rights and remedies under Subparagraphs (1), (2) and (4) of Subdivision (a) of Section 1951.2 of the California Civil Code of any amendment thereto), shall be entitled to recover from Tenant the worth at the time of award of the amount by which the unpaid rent for the balance of the term after the time of award exceeds the amount of such rental loss that the Tenant proves could be reasonably avoided. The worth at the time of award of the amount referred to in subparagraphs (1) and (2) of Subdivision (a) of Section 1951.2 of the California Civil Code shall be computed by allowing interest at the maximum rate allowed by law. The worth at the time of the award of the amount referred to in subparagraph (3) of Subdivision (a) of Section 1951.2 of the California Civil Code shall be computed by discounting such amount at the discount rate of the Federal Reserve Bank of San Francisco at the time of the award plus 1%.

    Any proof by Tenant of the amount of rental loss that could be reasonably avoided shall be made in the following manner: Landlord and Tenant shall each select a licensed real estate broker in the business of renting property of the same type and use as the premises and in the same geographic vicinity and such two real estate brokers shall select a third licensed real estate broker and the three licensed real estate brokers so selected shall determine the amount of rental loss that could be reasonably avoided for the balance of the term of this Lease after the time of award. The decision of the majority of said licensed real estate brokers shall be final and binding upon the parties hereto.

    Should Landlord, following any breach or default of this Lease by Tenant, elect to keep this Lease in full force and effect, with Tenant retaining the right to possession of the premises (notwithstanding the fact the Tenant may have abandoned the leased premises), then Landlord, besides the rights and remedies specified in Section 1951.4 of the California Civil Code "(lessor may continue lease in effect after lessee's breach and abandonment and recover rent

as it becomes due, if lessee has right to sublet or assign, subject only to reasonable limitations)" and all other rights and remedies Landlord may have at law or equity, shall have the right to enforce all of Landlord's rights and remedies under this Lease. Notwithstanding any such election to have this Lease remain in full force and effect, Landlord may at any time thereafter elect to terminate Tenant's right to possession of said premises and thereby terminate this Lease for any previous breach or default which remains uncured, or for any subsequent breach or default. If Tenant is in default even before the move-in date, Tenant shall be responsible for any loss, including, but not limited to the broker's commission, Tenant Improvement costs, rent, and any legal fees.

DESTRUCTION OR DAMAGE

27. (a) In the event the premises or a portion of the building is damaged by fire or other insured casualty, Landlord shall diligently repair the same to the extent possible with the insurance proceeds received by Landlord, subject to the provisions of this Section hereinafter set forth, if such repairs can in Landlord's opinion be made within 90 days after issuance of a building permit therefor under the laws and regulations of federal, state and local governmental authorities having jurisdiction thereof. In such event this Lease shall remain in full force and effect except that if such damage is not the result of the negligence or willful misconduct of Tenant or Tenant's agents, contractors, employees, subtenants, licensees, invitees or visitors, an abatement of basic rent shall be allowed Tenant for such part of the premises as shall be rendered unusable by Tenant in the conduct of its business during the time such part is so unusable. Notwithstanding the foregoing, if such damage shall occur during the final year of the term of this Lease, Landlord shall not be obligated to repair such damage, but may instead elect to terminate this Lease upon written notice given to Tenant within 30 days after the date of such fire or other casualty, in which event this Lease shall terminate as of the termination date specified in Landlord's notice.

(b) If such repairs cannot in Landlord's opinion be made within 90 days after issuance of a building permit therefor or if such damage is uninsured, Landlord may elect upon notice to Tenant given 60 days after the date of such fire or other casualty to (i) repair or restore such damage, in which event this Lease shall continue in full force and effect, but basic rent shall be partially abated as hereinabove in this Section provided or (ii) terminate this Lease in which event this Lease shall terminate as of the termination date specified in Landlord's notice.

(c) A total destruction of the building automatically shall terminate this Lease. Landlord and Tenant acknowledge that this Lease constitutes the entire agreement of the parties regarding events of damage or destruction, and Tenant waives the provisions of California Civil Code Section 1932(2) and 1933(4) and any similar statute now or hereafter in force.

(d) If the premises are to be repaired under this Section, Landlord shall repair at its cost any injury or damage to the building itself and the initial improvements made by Landlord. Tenant shall pay the cost of repairing or replacing all other improvements in the premises and Tenant's trade fixtures, furnishings, equipment and other personal property.

EMINENT DOMAIN

28. If all or any part of the premises shall be taken or appropriated by any public or quasi-public authority under the power of eminent domain, and such taking will substantially impair Tenant's use of the premises for more than 90 days, either party hereto shall have the right, at its option, to terminate this Lease. If all or any part of the building of which the premises are a part shall be taken or appropriated by any public or quasi-public authority under any power of eminent domain, Landlord may terminate this Lease. In either of such events, Landlord shall be entitled to and Tenant upon demand of Landlord shall assign to Landlord any rights of Tenant to any and all income, rent, award, or any interest therein whatsoever which may be paid or made in connection with such public or quasi-public use or purpose, and Tenant shall have no claim against Landlord or the condemnor for the value of any unexpired term of this Lease. If a part of the premises shall be so taken or appropriated and neither party hereto shall elect to terminate this Lease, the rent thereafter to be paid shall be equitably reduced.

PLATS AND RIDERS

29. Clauses, plats and riders, if any, signed by Landlord and Tenant and endorsed on or affixed to this Lease are a part hereof, and in the event of variation or discrepancy the duplicate original hereof, including such clauses, plats and riders, if any, held by Landlord shall control.

ESTOPPEL CERTIFICATES

30. At any time and from time to time, upon not more than ten (10) business days prior request by Landlord, Tenant shall execute, acknowledge and deliver to Landlord a statement certifying the date of commencement of this Lease, stating that this Lease is unmodified and in full force and effect (or if there have been modifications, that this Lease is in full force and effect as modified and the date and nature of such modifications) and the dates to which the rent has been paid, and setting forth such other matters as may reasonably be requested by Landlord. Landlord and Tenant intend that any such statement delivered pursuant to this paragraph may be relied upon by any mortgagee or the beneficiary of any Deed of Trust or by any purchaser or prospective purchaser of the building. Tenant hereby irrevocably appoints Landlord as its agent and attorney in-fact to execute, acknowledge and deliver any such certificate in the name of and on behalf of Tenant, in the event that Tenant fails to so execute, acknowledge and deliver any such certificate within 10 days after receipt thereof.

RIGHT OF LANDLORD TO PERFORM

31. All covenants and agreements to be kept or performed by Tenant under any of the terms of this Lease shall be performed by Tenant at Tenant's sole cost and expense and without any abatement of rent. If Tenant shall fail to pay any sum of money, other than rent, required to be paid by it hereunder or shall fail to perform any other act on its part to be performed hereunder, and such failure shall continue for ten (10) days after notice thereof by Landlord, Landlord may, but shall not be obligated to, and without waiving any default of Tenant or releasing Tenant from any obligations of Tenant hereunder, make any such payment or perform any such other act on Tenant's part to be made or performed as in this Lease provided. All sums so paid by the Landlord and all necessary incidental costs, together with interest thereon at the rate of ten percent (10%) per annum from the date of such payment by the Landlord, shall be paid to Landlord forthwith on demand, and Landlord shall have (in addition to any other right or remedy of Landlord) the same rights and remedies in the event of nonpayment thereof by Tenant as in the case of default by Tenant in payment of rent.

ATTORNEY FEES

32. If as a result of any breach or default on the part of Tenant under this Lease, Landlord uses the services of any attorney in order to secure compliance with this Lease, Tenant shall reimburse Landlord upon demand as additional rent for any and all reasonable attorneys' fees and expenses incurred by Landlord, whether or not formal legal proceedings are instituted. Should either party bring action against the other party, by reason of or alleging the failure of the other party to comply with any or all of its obligations hereunder, whether for declaratory or other relief, then the party which prevails in such action shall be entitled to its reasonable attorneys' fees and expenses related to such action, in addition to all other recovery or relief. A party shall be deemed to have prevailed in any such action (without limiting the generality of the foregoing) if such action is dismissed upon the payment by the other party of the sums allegedly due or the performance of obligations allegedly not complied with, or if such party obtains substantially the relief sought by it in the action, irrespective of whether such action is prosecuted to judgment. In addition, if either party to this Lease becomes a party to or is involved in any way in any action concerning this Lease or the premises by reason in whole or in part of any act, neglect, fault or omission of any duty by the other party, its employees or contractors, the party subjected to said involvement shall be entitled to reimbursement for any and all reasonable attorneys' fees and costs.

SURRENDER OF PREMISES

33. The voluntary or other surrender of this Least by Tenant or mutual cancellation thereof shall not work a merger and, at the option of Landlord, shall terminate all or any existing subleases or subtenancies, or at the option of Landlord, may operate as an assignment to Landlord of any or all such subleases or subtenancies.

WAIVER

34. The waiver by Landlord or Tenant of performance of any term, covenant or condition herein contained shall not be deemed to be a waiver of such term, covenant or condition or any subsequent breach of the same or any other term, covenant or condition herein contained. The subsequent acceptance of rent hereunder by Landlord shall not be deemed to be a waiver of any preceding breach by Tenant of any term, covenant or condition of this Lease, other than the failure of Tenant to pay the particular rent so accepted, regardless of Landlord's knowledge of such preceding breach at the time of acceptance of such rent.

NOTICES

35. All notices and demands which may or are required to be given by either party to the other hereunder shall be in writing. All notices and demands by Landlord to Tenant shall be delivered personally or sent by United States certified or registered mail, postage prepaid, addressed to Tenant at the premises, or to Valence Law Group, PC, 2855 Mitchell Drive, Suite 260, Walnut Creek, CA 94598 Fax: (415) 358-4570, krista@valencelaw.com, Attn: Krista Kim, or to such other place as Tenant may from time to time by like notice designate. All notices and demands by Tenant to Landlord shall be sent by United States certified or registered mail, postage prepaid, addressed to Landlord at King & Co. Investment Management Inc., 142 Sansome Street, Suite 600, San Francisco, CA 94104 or to such other place as Landlord may from time to time by like notice designate.

NOTICE OF SURRENDER

36. At least one hundred eighty (180) days before the last day of the term hereof, Tenant shall give to Landlord a written notice of intention to surrender the premises on that date, but nothing contained herein or any failure to give such notice shall be construed as an extension of the term hereof or as consent of Landlord to any holding over by Tenant.

DEFINED TERMS AND MARGINAL HEADINGS

37. The words “Landlord” and “Tenant”, as used herein shall include the plural as well as the singular words used in masculine gender include the feminine and neuter. If there be more than one Tenant, the obligations hereunder imposed upon Tenant shall be joint and several. The marginal headings and titles to the paragraphs of the Lease are not a part of this Lease and shall have no effect upon the construction or interpretation of any part hereof.

TIME AND APPLICABLE LAW

38. Time is of the essence of this Lease and each and all of its provisions. This Lease shall in all respects be governed by the laws of the state in which the premises are located.

SUCCESSORS

39. Subject to the provisions of Paragraph 16 hereof, the covenants and conditions herein contained shall be binding upon and inure to the benefits of the heirs, successors, executors, administrators and assigns of the parties hereto.

ENTIRE AGREEMENT

40. This Lease constitutes the entire agreement between Landlord and Tenant and no promises or representations, express or implied, either written or oral, not herein set forth shall be binding upon or inure to the benefit of Landlord or Tenant. This Lease shall not be modified by any oral agreement, either express or implied, and all modifications hereof shall be in writing and signed by both Landlord and Tenant.

REAL ESTATE BROKERS

41. Tenant represents and warrants that it has negotiated this Lease directly with the real estate broker(s) identified in the *Basic Lease Information* (the “**Broker**”) and has not authorized or employed, or acted by implication to authorize or to employ, any other real estate broker or salesman to act for Tenant in connection with this Lease. Tenant shall indemnify, defend and hold Landlord harmless from and against any and all claims by any real estate broker or salesman other than the Broker for a commission, finder’s fee or other compensation as a result of Tenant’s entering into this Lease. Tenant’s broker will be paid a commission equal to $2.00 per square foot per year. Commission to be paid fifty percent (50%) upon lease execution and fifty percent (50%) upon lease commencement. Any commission payable to Landlord’s Broker shall be payable pursuant to a separate agreement between Landlord and Landlord’s Broker.

AUTHORIZATION

42. Each individual executing this Lease on behalf of Tenant represents and warrants that he or she is duly authorized to execute and deliver this Lease on behalf of Tenant and that such execution is binding upon Tenant.

ADDITIONAL PROVISIONS

43. The exhibits and addenda listed below are incorporated by reference in this Lease.

REQUIRED DISCLOSURES RELATED TO ACCESSIBILITY STANDARDS

44. For purposes of Section 1938 of the California Civil Code, Landlord hereby discloses to Tenant, and Tenant hereby acknowledges, that the Premises have not undergone inspection by a Certified Access Specialist (CASp). As required by Section 1938(c) of the California Civil Code, Landlord hereby states as follows: "A Certified Access Specialist (CASp) can inspect the subject premises and determine whether the subject premises comply with all of the applicable construction-related accessibility standards under state law. Although state law does not require a CASp inspection of the subject premises, the commercial property owner or lessor may not prohibit the lessee or tenant from obtaining a CASp inspection of the subject premises for the occupancy or potential occupancy of the lessee or tenant, if requested by the lessee or tenant. The parties shall mutually agree on the arrangements for the time and manner of the CASp inspection, the payment of the fee for the CASp inspection, and the cost of making any repairs necessary to correct violations of construction-related accessibility standards within the premises." In furtherance of the foregoing, Landlord and Tenant hereby agree as follows: (a) any CASp inspection requested by Tenant shall be conducted, at Tenant's sole cost and expense, by a CASp designated by Landlord; and (b) pursuant to the terms of Article 13 hereof, Tenant, at its cost, is responsible for making any repairs within the Premises to correct violations of construction-related accessibility standards; and, if anything done by or for Tenant in its use or occupancy of the Premises shall require repairs to the Building (outside the Premises) to correct violations of construction-related accessibility standards, then Tenant shall, at Landlord's option, either perform such repairs at Tenant's sole cost and expense or reimburse Landlord upon demand, as additional rent, for the cost to Landlord of performing such repairs.

    Landlord and Tenant hereby acknowledge that prior to the execution of this Lease, Landlord and Tenant executed a Disability Access Obligations Notice pursuant to San Francisco Administrative Code Chapter 38. In addition, Tenant acknowledges receipt from Landlord of an Access Information Notice in Tenant's requested language as required by San Francisco Administrative Code Chapter 38, and Tenant hereby confirms that Tenant's requested language is English. Tenant acknowledges that such notices comply with the requirements of San Francisco Administrative Code Chapter 38.

FACSIMILE SIGNATURES

45. The parties shall be bound by their signatures transmitted by facsimile or electronic mail (in pdf format) as if such signatures were original "ink" signatures. They further agree to forward original "ink" signatures promptly following the transmission of signatures by facsimile or electronic mail. This Agreement shall be enforceable with facsimile signatures or electronically-transmitted signatures if one or more parties does not deliver an original signature.

[Signatures appear on the following page]

IN WITNESS WHEREOF Landlord and Tenant have executed this Lease the day and year first above written.

LANDLORD	**TENANT**
By: King Family Irrevocable Trust	By: 89bio, Inc. (a Delaware Corporation)
/s/ Shirley King	/s/ Ryan Martins
By: Shirley King	By: Ryan Martins
Its: Trustee	Its: Chief Financial Officer
Date: 12/9/2019	Date: 12/9/2019

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in Registration Statement No. 333-235577 on Form S-8 of our report dated March 18, 2020, relating to the financial statements of 89bio, Inc. appearing in this Annual Report on Form 10-K for the year ended December 31, 2019.

/s/ Deloitte & Touche LLP

San Francisco, California
March 18, 2020

Exhibit 23.2

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in Registration Statement No. 333-235577 on Form S-8 of our report dated August 15, 2019, except for the retroactive effect of both the 1-for-6.217 reverse stock split and the reorganization, as described in Note 1, as to which the date is October 28, 2019, relating to the financial statements of 89bio, Inc. (operating as 89Bio Ltd. prior to the reorganization described in Note 1), appearing in this Annual Report on Form 10-K for the year ended December 31, 2019.

/s/ Brightman Almagor Zohar & Co.
A Firm in the Deloitte Global Network

Tel Aviv, Israel
March 18, 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, Rohan Palekar, certify that:

1. I have reviewed this Annual Report on Form 10-K of 89bio, 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. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the registrant and have:

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

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

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

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

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

Date: March 18, 2020

By: /s/ Rohan Palekar

Rohan Palekar
Chief Executive Officer
(principal executive officer)

Exhibit 31.2

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, Ryan Martins, certify that:

1. I have reviewed this Annual Report on Form 10-K of 89bio, 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. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-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 our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

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

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

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

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

Date: March 18, 2020

By: /s/ Ryan Martins

Ryan Martins
Chief Financial Officer
(principal financial and accounting officer)

Exhibit 32.1

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

In connection with the Annual Report of 89bio, Inc. (the "Company") on Form 10-K for the year ending December 31, 2019, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), each of the undersigned officers of the Company hereby certifies, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that to the best of his knowledge:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 18, 2020 By: /s/ Rohan Palekar

Rohan Palekar
Chief Executive Officer
(principal executive officer)

Date: March 18, 2020 By: /s/ Ryan Martins

Ryan Martins
Chief Financial Officer
(principal financial and accounting officer)

The foregoing certification is being furnished solely to accompany the Report pursuant to 18 U.S.C. §1350, and is not being filed for purposes of Section 18 of the Securities Exchange Act of 1934, and is not to be incorporated by reference into any filing of the Company, whether made before or after the date hereof, regardless of any general incorporation language in such filing.
Note: A signed original of this written statement required by §906 has been provided to 89bio, Inc. and will be retained by 89bio, Inc. and furnished to the Securities and Exchange Commission or its staff upon request.