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, 2024
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.)**
655 Montgomery Street, Suite 1500 San Francisco, California	**94111**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (415) 432-9270

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 has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☒

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

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant (based on the closing price of such stock on The Nasdaq Global Market on June 28, 2024, the last business day of the registrant's most recently completed second fiscal quarter) was approximately $722.4 million. 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 number of shares of the registrant's common stock outstanding as of February 24, 2025 was 145,984,182.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's proxy statement for the 2025 Annual Meeting of Stockholders, to be held on or about May 28, 2025, are incorporated by reference into Part III of this Annual Report on Form 10-K to the extent stated herein. Such proxy statement will be filed with the Securities and Exchange Commission within 120 days of the registrant's fiscal year ended December 31, 2024.

Auditor Firm Id: 185 Auditor Name: KPMG LLP Auditor Location: San Francisco, California, USA

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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 pegozafermin or any future product candidates;
- our ongoing and planned clinical trials;
- the timing of and our ability to obtain regulatory approvals for pegozafermin or any future product candidates;
- our estimates regarding expenses, future revenue, capital requirements, needs for additional financing, and the sufficiency of our existing cash, cash equivalents and marketable securities;
- our ability to obtain additional capital;
- supply chain interruptions, delays in patient enrollment or other delays in our clinical trials;
- 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 pegozafermin or any future product candidates, if approved;
- our commercialization, marketing and manufacturing capabilities and strategy;
- the expected potential benefits of strategic collaboration with third parties and our ability to attract collaborators with development, regulatory and commercialization expertise;
- substantial competition in our industry and with respect to the product candidates that we are developing;
- regulatory actions with respect to our product candidates or our competitors' products and product candidates;
- 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;
- our inability to comply with, and the effect on our business of, evolving legal standards and regulations, including concerning data protection and consumer privacy and sustainability;
- geopolitical instability, such as the ongoing conflict in Ukraine, the conflict in Israel and surrounding areas and the rising tensions between China and Taiwan, and the macroeconomic environment, including inflationary pressures, general economic slowdown or a recession, rising interest rates, changes in monetary

policy, instability in financial institutions, and changes in trade policies, including tariffs or other trade restrictions or the threat of such actions;

- our failure to maintain effective internal controls; and
- the risk that our business, financial condition and results of operations may be adversely affected by other political, economic, business and competitive factors.

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, pegozafermin, a specifically engineered glycoPEGylated analog of fibroblast growth factor 21 ("FGF21"), is currently being developed for the treatment of metabolic dysfunction-associated steatohepatitis ("MASH"), previously known as nonalcoholic steatohepatitis, and for the treatment of severe hypertriglyceridemia ("SHTG").

MASH is a severe form of metabolic dysfunction-associated steatotic liver disease ("MASLD"), previously known as nonalcoholic fatty liver disease, and is characterized by inflammation and fibrosis in the liver that can progress to cirrhosis, liver failure, hepatocellular carcinoma ("HCC") and death. In 2020 and 2022, we presented positive topline results from our Phase 1b/2a trial of pegozafermin in MASH patients. In March 2023, we reported positive topline 24-week data from our Phase 2b ENLIVEN trial of pegozafermin including fibrosis benefits in both non-cirrhotic (F2-F3) and compensated cirrhotic (F4) MASH patients. In the ENLIVEN trial, patients received weekly doses or an every-two-week dose of pegozafermin or placebo for 24 weeks followed by a blinded extension phase of an additional 24 weeks for a total treatment period of 48 weeks. The 44 mg every-two-week and the 30 mg weekly dose groups both met, with high statistical significance, both of the primary histology endpoints per the U.S. Food and Drug Administration ("FDA") guidance definitions on endpoints for accelerated approval in non-cirrhotic MASH patients. In September 2023, the FDA granted Breakthrough Therapy designation to pegozafermin in patients with MASH. In November 2023, we announced positive topline data from the blinded extension phase of our ENLIVEN trial at 48 weeks. Both the 44 mg every-two-week and 30 mg weekly dose groups demonstrated statistically significant improvements across Non-Invasive Tests ("NITs") representing key markers of liver health. The benefits observed at week 48 represented by NITs were consistent with the histology and NITs results observed at week 24, indicating sustained benefits over time.

In December 2023, we held successful end-of-Phase 2 meetings with the FDA, supporting the advancement of pegozafermin into a Phase 3 program and future biologics license application ("BLA") filing. We also received scientific advice from the European Medicines Agency ("EMA"), which generally aligned with the feedback from the FDA. In March 2024, the EMA granted Priority Medicines ("PRIME") designation to pegozafermin in patients with MASH based on clinical data from the ENLIVEN trial.

The Phase 3 program (ENLIGHTEN) is comprised of two Phase 3 trials evaluating pegozafermin in patients with MASH: (i) ENLIGHTEN-Fibrosis, in patients with fibrosis stage F2-F3 (F2-F3), which we initiated in March 2024, and (ii) ENLIGHTEN-Cirrhosis, in patients with compensated cirrhosis (F4), which we initiated in May 2024.

We expect to report topline data from the histology cohorts of the ENLIGHTEN-Fibrosis and the ENLIGHTEN-Cirrhosis trial in the first half of 2027 and in 2028 respectively. These data are intended to support the filing for accelerated approval and conditional approval for non-cirrhotic (F2-F3) and compensated cirrhotic (F4) MASH in the United States and Europe, based on previously obtained alignment with the FDA and EMA.

We are also developing pegozafermin for the treatment of SHTG. In June 2022, we announced positive topline results from the Phase 2 trial of pegozafermin in SHTG patients (ENTRIGUE). SHTG is a condition identified by severely elevated levels of triglycerides (≥500 mg/dL), which is associated with an increased risk of MASH, cardiovascular events and acute pancreatitis. The ENTRIGUE trial met its primary endpoint demonstrating statistically significant and clinically meaningful reductions in triglycerides from baseline and key secondary endpoints. We received feedback from the FDA supporting the advancement of pegozafermin and initiated our Phase 3 trial in SHTG patients (ENTRUST), the first of two recommended Phase 3 trials, in the second quarter of 2023. In December 2024, we completed enrollment in the ENTRUST trial with a total of 369 patients. We expect to report topline data from this trial in the first quarter of 2026. Safety data from the ongoing SHTG Phase 3 program is expected to support the safety database requirements for MASH and vice versa.

FGF21 is an anti-fibrotic metabolic hormone that regulates energy expenditure and glucose and lipid metabolism. FGF21 analogs represent a promising class of drugs to treat MASH, because they not only address the liver manifestations, but also have an effect on the multiple co-morbidities that worsen MASH. The FGF21 class of drugs have shown the ability to reverse fibrosis in patients with compensated cirrhosis marking it the first class of drugs to show this benefit in this patient population, who have the highest unmet need in MASH. FGF21 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. 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. 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 pegozafermin to extend the half-life of the molecule while maintaining potency and thereby the clinical benefits of FGF21.

Pegozafermin may be a differentiated FGF21 therapy based on its robust and durable biological effects, a favorable tolerability profile and its potential for every-two-week dosing. Given its ability to address the key liver pathologies in MASH, as well as the underlying metabolic dysregulation in MASH patients, pegozafermin has the potential to become a backbone of treatment in MASH, including in compensated cirrhotic (F4) patients. Pegozafermin is the only FGF21 analog being developed for the treatment of SHTG and its broad metabolic effects could potentially differentiate it from competitors in this market. Pegozafermin has a long half-life which allows convenient weekly or every-two-week dosing and is currently the only FGF21 analog being tested in Phase 3 trials with every-two-week dosing. The convenient dosing regimen may support adoption and compliance amongst patients living with these chronic and generally asymptomatic diseases. Pegozafermin is self-administered by patients subcutaneously in a liquid formulation using a pre-filled syringe.

Our Strategic Priorities

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 by focusing on our strategic priorities, which include rapidly advancing pegozafermin through clinical development for the treatment of MASH, progressing the development of pegozafermin for the treatment of SHTG, scaling-up and optimizing the manufacturing of pegozafermin and establishing a commercial infrastructure in key geographies.

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 MASH 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, pegozafermin, a specifically engineered glycoPEGylated analog of FGF21, for the treatment of MASH and SHTG. We believe pegozafermin is an ideal candidate for the treatment of MASH based on its ability to address the key liver pathologies in MASH through the reversal of fibrosis and cirrhosis, as well as its ability to address the underlying metabolic dysregulation in MASH patients, its favorable tolerability profile, and its potential for a longer dosing interval. Multiple epidemiological studies have linked MASLD to increased cardiovascular disease, concluding that the majority of deaths among MASLD patients are attributable to cardiovascular disease. As a result, we believe it is important that new therapeutics options for MASH address the underlying cardiovascular and metabolic dysregulations in these patients. We are also developing pegozafermin for the treatment of SHTG given the potential of pegozafermin to meaningfully reduce triglycerides. Pegozafermin may have a competitive differentiation from approved therapies and other molecules in development based on its impact on improving liver fat and other metabolic markers in addition to triglyceride reduction.

Disease Overview – MASH

MASH, a severe form of MASLD, 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.

MASH represents a large and rapidly growing problem in the United States and worldwide. Diagnoses have been on the rise and are expected to increase dramatically in the next decade. The prevalence of MASLD, which affects approximately 25% of the global population, and MASH, which develops in approximately 20% to 25% of MASLD patients, is driven primarily by the worldwide obesity epidemic. As a result, the prevalence of MASH has increased significantly in recent decades, paralleling similar trends in the prevalence of obesity, insulin resistance and Type 2 diabetes. 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. While increased use of incretin-based therapies will likely reduce the overall prevalence of MASH, we anticipate the target patient population to be treated to increase as diagnosis rates will increase with the approval of new therapies. In 2024, Rezdiffra™, developed by Madrigal Pharmaceuticals, Inc., received regulatory approval for the treatment of non-cirrhotic MASH.

The critical pathophysiologic mechanisms underlying the development and progression of MASH include reduced ability to handle lipids, increased insulin resistance, injury to hepatocytes and liver fibrosis in response to hepatocyte injury. MASH patients have an excessive accumulation of fat in the liver resulting primarily from a caloric intake above and beyond energy needs. A healthy liver contains less than 5% fat, but a liver in someone with MASH can contain more than 20% fat. This abnormal liver fat contributes to the progression to MASH, a liver necro-inflammatory state, that can lead to scarring, also known as fibrosis, and, for some, can progress to cirrhosis and liver failure—cirrhosis develops in approximately 20% to 45% of patients. In some cases, cirrhosis progresses to decompensated cirrhosis with attendant severe morbidity and risk of death from end stage liver disease. In addition, it is estimated that 8% of patients with advanced fibrosis will develop HCC. MASH is a complex, multifaceted disease that doesn't just affect the liver. Patients with MASH 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.

Disease Overview – SHTG

We are also developing pegozafermin for the treatment of SHTG. Hypertriglyceridemia ("HTG") is characterized by elevated fasting plasma triglyceride levels > 200 mg/dL and SHTG is typically defined as triglyceride levels of ≥ 500 mg/dL. SHTG is associated with an increased risk of MASLD, MASH and cardiovascular diseases, as well as acute pancreatitis, accounting for up to 10% of all acute pancreatitis episodes. A 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 4 million patients in the United States with triglyceride levels of ≥ 500 mg/dL of which approximately 800,000 patients are inadequately treated with existing therapies and are thereby at increased risk for acute pancreatitis and atherosclerotic cardiovascular events. Of these patients, it is estimated that up to 100% have clinically meaningful hepatic fat using magnetic resonance imaging – proton density fat factor ("MRI-PDFF") definition of ≥ 5% fat fraction (baseline data from the sub-study in ENTRIGUE; n=24), up to 70% have Type 2 diabetes, and dyslipidemia was commonly observed. 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 triglyceride levels, similar to the focus today of physicians on managing LDL-c levels, as well as the commercial efforts of other companies that are expected to promote triglyceride 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. Despite multiple agents approved for the treatment of SHTG, these agents have limitations that may not make them ideal for all patients. 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 for

pegozafermin as an add-on therapy along with the opportunity for pegozafermin to be used in patients not on any background therapy. Given the continuing unmet need in SHTG and limitations of current treatments, there are other novel agents in development for the treatment of SHTG, including APOC3 inhibitors.

Diagnosis of MASH

Most people with MASH 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 MASH, which necessitates the joint presence of steatosis, ballooning and lobular inflammation. Once pathologically confirmed, the severity of MASLD and MASH is determined using the histologically validated MASLD activity score ("MAS"), which grades disease activity on a scale of 0 to 8. The MAS 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 MASH 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. Additionally, histology diagnosis is confounded by evaluation of a small sliver of a large heterogenous organ that may not represent the full organ, and significant variability in reading of slides including inter- and intra-reader variability. Several non-invasive tools such as clinical risk scores, serum markers and imaging techniques are increasingly used to assess MASH patients. NITs, such as the Fibroscan-AST ("FAST") score, Fibrosis-4 index, the Enhanced Liver Fibrosis score and vibration-controlled transient elastography, ("VCTE"), have been validated and are increasingly used. These NITs 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. In 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 NITs, along with recent regulatory approvals for MASH treatments, will result in an increase in the diagnosis and treatment rates for MASH in the future.

FGF21 Overview

Fibroblast growth factors ("FGFs"), including FGF21, 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, 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.

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 de novo lipogenesis (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 MASH in multiple clinical trials.

Improving Liver Inflammation and Fibrosis

FGF21 is also believed to reduce liver fibrosis, the pathological change most clearly linked to liver-related morbidity in MASH 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 demonstrated an improvement in liver fibrosis in patients in MASH in a clinical trial.

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. 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.

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 MASH. FGF21 is not believed to activate FGFR4. Activation of FGFR4 results in an increase in LDL cholesterol and has been implicated in the etiology or progression of HCC.

Pegozafermin Overview

We are developing pegozafermin, a specifically engineered glycoPEGylated analog of FGF21, for the treatment of MASH and SHTG. Pegozafermin has been specifically engineered to retain the activity of native FGF21 while extending its half-life. Specifically, it has been 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 pegozafermin 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 Pegozafermin

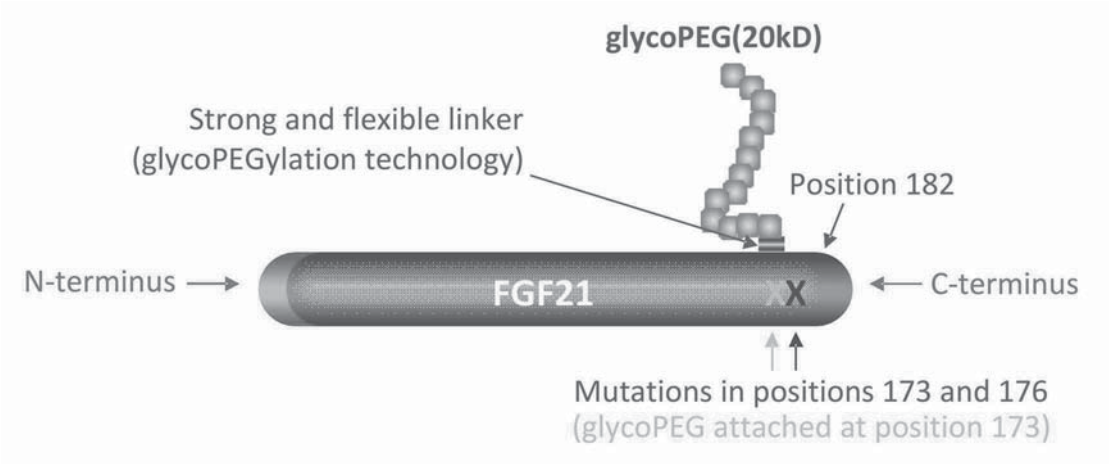
Pegozafermin has been optimally constructed with two mutations via substitutions with natural amino acids at site-specific positions (173 and 176) toward the C-terminus end of the hormone. The mutations were incorporated into the FGF21 sequence after existing proline to create a consensus sequence for 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.

Pegozafermin 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. Figure 1 below shows the structure of pegozafermin.

Figure 1: Structure of Pegozafermin



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. Similar moles of FGF21 are delivered with pegozafermin 30mg and efruxifermin 50mg.

Pegozafermin 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.

Figure 2: Summary of Pegozafermin 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 to remain intact, further reducing degradation	▪ Further enhances half-life

Phase 1a and Phase 1b/2a Trials

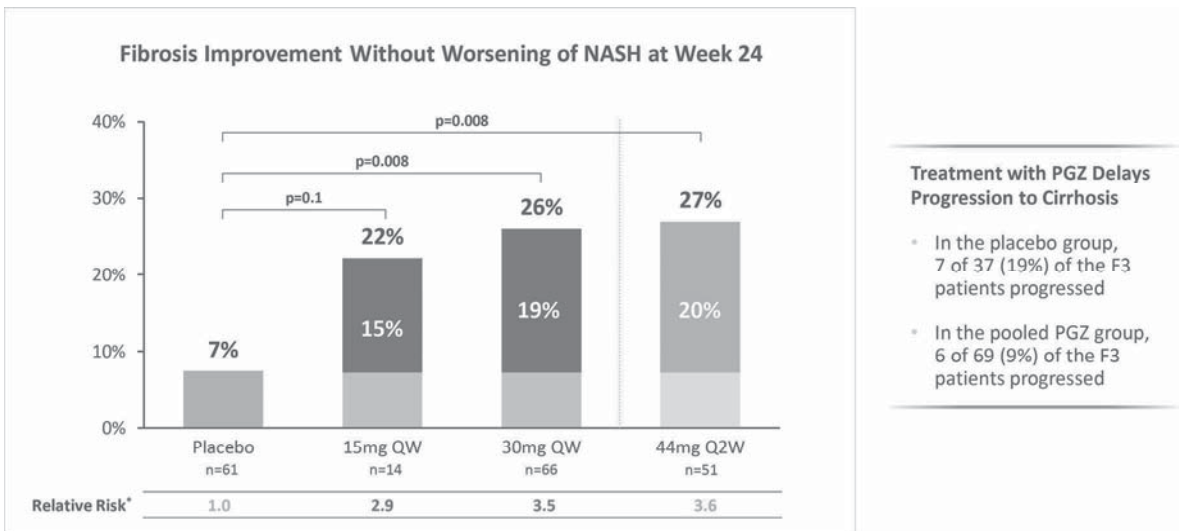
We have conducted Phase 1a and Phase 1b/2a clinical trials for pegozafermin in healthy volunteers and patients with MASH. In our Phase 1a clinical trial, pegozafermin was well tolerated and there were no deaths, serious adverse events or discontinuations due to adverse events. In 2020 and 2022, we presented positive topline results from cohorts 1 to 6 and cohort 7, respectively, in our Phase 1b/2a trial in MASH patients.

Phase 2b (ENLIVEN) Trial in Fibrosis Stage 2 or 3 MASH Patients

ENLIVEN was a multicenter, randomized, double-blind, placebo-controlled Phase 2b trial in biopsy-confirmed MASH patients with fibrosis stage 2 or 3 and NAS ≥ 4. The trial enrolled a total of 219 patients who receive either a weekly dose (15 mg or 30 mg) or an every-two-week dose (44 mg) of pegozafermin in a liquid formulation or placebo for 24 weeks with a randomization schema of 4: 4: 2.5: 1 (placebo: 30 mg QW: 44 mg Q2W: 15 mg QW). All patients continued treatment in a blinded extension phase for 24 weeks for a total treatment period of 48 weeks, with some of the placebo patients re-randomized to receive pegozafermin in the extension phase. The primary analysis evaluated the effect of pegozafermin on the two FDA approvable histology endpoints, 1-point fibrosis improvement with no worsening of MASH and MASH resolution with no worsening of fibrosis, and included F2/F3 patients who met histologic entry criteria and MAS ≥ 4 based on the three-panel consensus read of biopsies at baseline to ensure consistency between baseline and end of treatment biopsy reading methods.

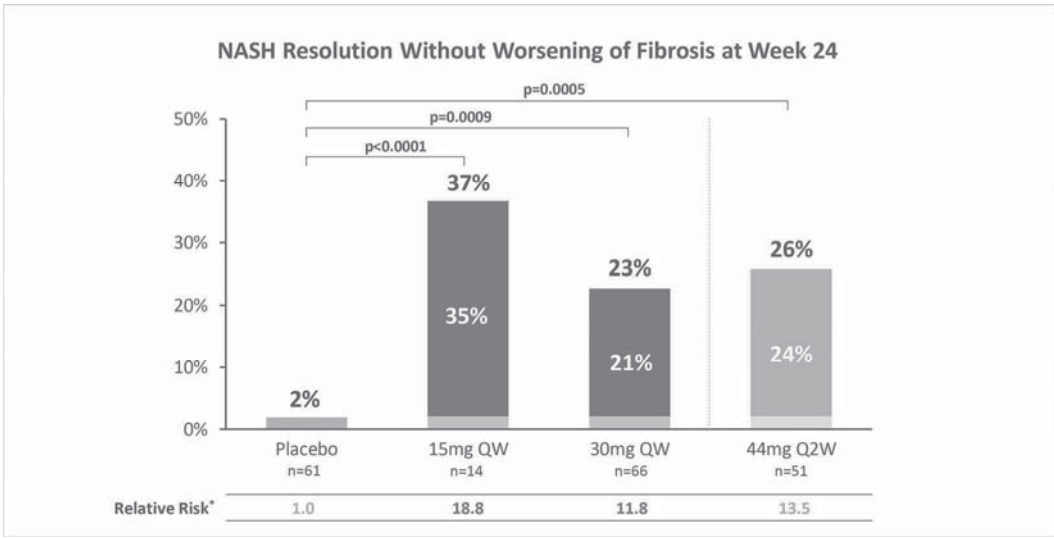
We reported topline data from ENLIVEN in March 2023. The 44 mg every-two-week and the 30 mg weekly dose groups both met, with high statistical significance, both of the primary histology endpoints per FDA guidance on endpoints for accelerated approval in non-cirrhotic MASH patients. The 44 mg every-two-week and the 30 mg weekly dose groups both demonstrated at least one-stage fibrosis improvement without worsening of MASH (27% and 26%, respectively) at 3.5 times the placebo rate (7%), or also known as relative risk, as reflected in Figure 3 below.

Figure 3: Fibrosis Improvement Without Worsening of MASH at Week 24



As seen in Figure 4 below, the 44 mg every-two-week and the 30 mg weekly dose groups both demonstrated MASH resolution without worsening of fibrosis of 26% and 23%, respectively, which is between 12 to 14 times the placebo rate (2%), or also known as relative risk.

Figure 4: MASH Resolution Without Worsening of Fibrosis at Week 24



These dose groups also demonstrated statistically significant and clinically meaningful improvements in liver fat, non-invasive markers of liver fibrosis and inflammation as well as meaningful improvements in other metabolic and lipid markers. Pegozafermin was generally well tolerated with a favorable safety profile consistent with prior studies. Across dose groups, the most common adverse events (AEs) were Grade 1 or 2 gastrointestinal events (diarrhea, nausea and increased appetite), most of which were mild to moderate in nature. No clinically relevant or statistically significant effects relative to placebo on bone mineral density measured by DEXA scans, bone biomarkers or vital signs were noted at week 24.

The ENLIVEN trial also included 14 biopsy-confirmed MASH patients with compensated cirrhosis (F4 patients) who were not part of the primary analysis but continued in the study. 12 of these 14 patients underwent a follow-up biopsy at week 24. In a descriptive analysis of these data, five out of 11 pegozafermin-treated patients experienced at least one-stage improvement in liver fibrosis with no worsening of MASH by week 24 compared with zero out of 1 patient on placebo. An additional two pegozafermin-treated patients experienced at least one-stage improvement in liver fibrosis with no worsening of ballooning or inflammation.

Results from the ENLIVEN trial were published in the New England Journal of Medicine. Additional data included in these publications showed that treatment with pegozafermin resulted in significant benefit across several key sub populations of MASH patients, and adding pegozafermin to patients taking GLP-1 therapies improved key MASH measures.

Long-term Data from Phase 2b (ENLIVEN) Trial

In November 2023, we announced positive topline data from the blinded extension phase of our ENLIVEN trial evaluating treatment with pegozafermin in patients with MASH. At week 48, both the 44 mg every-two-week and 30 mg weekly dose groups demonstrated statistically significant improvements across key markers of liver health. The benefits observed at week 48 were consistent with the results observed at week 24, indicating sustained benefits over time.

ENLIVEN Extension Data

Patients in ENLIVEN continued in a blinded extension phase for an additional 24 weeks (the "Extension Phase") past the primary endpoint at week 24 (the "Main Study"), for a total treatment period of 48 weeks. A subset of patients in the placebo arm of the Main Study (n=19) were re-randomized to receive 30 mg of pegozafermin weekly during the Extension Phase. The efficacy endpoints assessed in the Extension Phase included liver fat, non-

invasive markers of fibrosis and inflammation, and metabolic markers. Per the protocol, these patients did not undergo biopsies at week 48.

Figure 5. Extension Phase Data at Week 48: Liver Non-Invasive Tests (NITs) Results [marker of]

		Pegozafermin	
	Placebo	30mg QW	44mg Q2W
F2-F3 Patients	(n=35)[1, 2]	(n=50)[2]	(n=45)[2]
MRI-PDFF [liver fat] [4]	-11%	-60%**	-47%*
ALT [liver injury/inflammation][3]	-11%	-42%***	-35%**
AST [liver injury/inflammation][3]	-4%	-39%***	-36%***
ELF score [liver fibrosis][3]	+0.1	-0.3**	-0.4***
Pro-C3 [collagen deposition][3]	+5%	-15%***	-14%***
VCTE (kPa) [liver stiffness][4]	-0.8	-2.9*	-1.3
FAST [liver fibrosis][3]	-4%	-59%***	-51%***

***p<0.001, **p<0.01, *p<0.05 versus placebo.
[1] Dataset excludes 19 placebo patients who were re-randomized to pegozafermin 30mg QW in the Extension Phase.
[2] Extension data at week 48 represents patients who entered the blinded Extension Phase.
[3] Least Square (LS) mean change from baseline.
[4] Median change from baseline.

Patients on Background GLP-1 Therapy:

Consistent with results observed in the Main Study, patients on background GLP-1 therapy who received pegozafermin continued to derive a greater benefit on markers of liver fibrosis, liver injury/inflammation, liver fat and lipids, compared to patients who continued GLP-1 therapy in the placebo group. Patients entering ENLIVEN on background GLP-1 therapies were required to have been on a stable regimen for at least six months.

Figure 6. Extension Phase Data at Week 48: Patients on Background GLP-1, Liver NITs and Lipids Results [marker of]

	Placebo (n=12)	Pegozafermin[3] (n=26)
MRI-PDFF [liver fat][2]	-34%	-53%
ALT [liver injury/inflammation][1]	-15%	-44%
AST [liver injury/inflammation] [1]	-11%	-42%
ELF score [liver fibrosis] [1]	0	-0.5
Pro-C3 [collagen deposition][1]	-9%	-19%
VCTE (kPa) [liver stiffness][2]	-3.2	-2.2
FAST [liver fibrosis] [1]	-43%	-52%
Triglycerides [lipids][2]	-12%	-22%
LDL-C [lipids][2]	-5%	-14%

[1] LS mean change from baseline.
[2] Median change from baseline.
[3] Patients dosed with pegozafermin 30mg QW or 44mg Q2W.

Compensated Cirrhosis (F4) Patients:

Biopsy-confirmed compensated cirrhosis F4 patients who had previously demonstrated histological response and improvement across NITs at week 24 continued to demonstrate robust and sustained improvements in non-invasive measures at week 48.

Figure 7. Extension Phase Data at Week 48: F4 Patients, Liver NITs Results [marker of]

	Pegozafermin[3] (n=12)
ALT [liver injury/inflammation][1]	-58%
AST [liver injury/inflammation][1]	-38%
ELF score [liver fibrosis][1]	-0.5
Pro-C3 [collagen deposition][1]	-20%
VCTE (kPa) [liver stiffness][2]	-1.1
FAST [liver fibrosis][1]	-42%

[1] LS mean change from baseline.
[2] Median change from baseline.
[3] Patients dosed with pegozafermin 15mg QW, 30mg QW or 44mg Q2W.

Pegozafermin continued to demonstrate a favorable safety and tolerability profile at week 48, consistent with previously reported data. The most common treatment-emergent adverse events were Grade 1 or 2 gastrointestinal events. Incidence rates of adverse events remained generally stable between week 24 and week 48 with no new patients on pegozafermin reporting diarrhea or nausea during the Extension Phase. At week 48, no clinically meaningful or statistically significant changes in bone mineral density or bone biomarkers were observed relative to placebo. No clinically meaningful or statistically significant changes in blood pressure or heart rate were observed relative to placebo.

Phase 3 (ENLIGHTEN) Program

In December 2023, we held a successful end-of-Phase 2 meeting with the FDA, supporting the advancement of pegozafermin into a Phase 3 program and future BLA filing. We also received scientific advice from the EMA, which generally aligned with the feedback from the FDA. The Phase 3 ENLIGHTEN program is comprised of two randomized, double-blinded, placebo-controlled Phase 3 trials evaluating pegozafermin in patients with MASH: (i) ENLIGHTEN-Fibrosis, in patients with fibrosis stage F2-F3 (F2-F3), which we initiated in March 2024 and (ii) ENLIGHTEN-Cirrhosis, in patients with compensated cirrhosis (F4), which we initiated in May 2024.

We expect to report topline data from the histology cohorts of the ENLIGHTEN-Fibrosis and the ENLIGHTEN-Cirrhosis trial in the first half of 2027 and in 2028 respectively. These data are intended to support the filing for accelerated approval and conditional approval for non-cirrhotic (F2-F3) and compensated cirrhotic (F4) MASH in the United States and Europe, based on previously obtained alignment with the FDA and EMA.

ENLIGHTEN-Fibrosis

- ENLIGHTEN-Fibrosis is enrolling patients with F2-F3 MASH. The trial is designed to evaluate the efficacy and safety of pegozafermin administered 30 mg weekly and 44 mg every-two-weeks.
    - Histology Cohort: The co-primary endpoints will be a one-point improvement in fibrosis with no worsening of MASH and MASH resolution with no worsening of fibrosis. These endpoints will be assessed at week 52 and are intended to support a filing for accelerated approval in the United States and conditional approval in Europe in F2-F3 patients, based on previously obtained alignment with the respective regulatory authorities. Topline results from the histology cohort of the trial are expected in the first half of 2027.
    - Outcomes: Patients will continue to be treated in a blinded extension phase to measure clinical outcomes to support full approval in F2-F3 patients. The clinical outcome events are expected to be primarily due to progression to cirrhosis.

ENLIGHTEN-Cirrhosis

- ENLIGHTEN-Cirrhosis is enrolling patients with compensated F4 MASH. The trial is designed to evaluate the efficacy and safety of pegozafermin administered 30 mg weekly.
    - Histology Cohort: The primary endpoint will be regression of fibrosis from F4 to an earlier stage of fibrosis. This endpoint is planned to be assessed at 24 months. This primary endpoint is

intended to support a filing for accelerated approval in the United States and conditional approval in Europe in F4 patients, based on previously obtained alignment with the respective regulatory authorities. Topline results from the histology cohort of the trial are expected in 2028.

- Outcomes: Patients will continue to be treated in a blinded extension phase through clinical outcome events that are expected to be predominantly decompensation events. Alignment with the FDA on modified definitions of some of these events could allow the trial to reach the final number of events quicker and therefore accelerate the timeline to trial readout. Positive results would support full approval in F4 patients and will also serve as confirmatory full approval in F2-F3 patients.

Both ENLIGHTEN-Fibrosis and ENLIGHTEN-Cirrhosis are expected to enroll a significant proportion of patients on stable doses of GLP-1 based therapies and data from these patients in the trials will evaluate the expected incremental benefit of adding pegozafermin to these therapies. Patients will be stratified in both trials for GLP-1-based therapy usage. Both trials will employ the three-panel consensus biopsy reading methodology, which was successfully utilized in the ENLIVEN trial, for both baseline and primary endpoint biopsy reads. Patients will self-administer pegozafermin using the planned commercial liquid formulation delivered as a single subcutaneous injection.

Pegozafermin Clinical Development in SHTG

In June 2022, we reported positive topline results from our Phase 2 clinical trial (ENTRIGUE) of pegozafermin in SHTG patients. Results demonstrated statistically significant reductions in median triglycerides (TG) from baseline across all dose groups treated with pegozafermin compared to placebo after 8 weeks. Additionally, results were consistent in patients not on background therapy or on background therapy (consistent results on statins or statin combos, prescription fish oils, and fibrates) and across various subgroups, including those with the greatest disease burden, such as Type 2 diabetes and baseline TG levels ≥ 750 mg/dL.

Phase 3 (ENTRUST) Trial of Pegozafermin in SHTG Patients

In 2022, we received feedback from the FDA supporting the advancement of pegozafermin into Phase 3 for the treatment of SHTG. The FDA agreed with the proposed primary endpoint of reduction in triglycerides (TG) from baseline without the need for a clinical outcome study. The FDA also agreed to the proposed doses and proposed secondary endpoints and were generally aligned with other trial parameters. Since SHTG is a common, chronic condition and pegozafermin is a novel investigational biologic therapy, the agency requires two Phase 3 trials in SHTG, each of one year duration as part of the efficacy and safety database required to support the registration package.

In May 2023, we initiated the ENTRUST trial, the first of two recommended Phase 3 trials in SHTG. ENTRUST is a randomized, double-blind, placebo-controlled global trial that planned to enroll up to 360 SHTG patients randomized in a 3:3:2 ratio of pegozafermin (30 mg, 20 mg or placebo) given once weekly (“QW”) by subcutaneous injection for 52 weeks.

The primary endpoint is the percent change from baseline in fasting triglycerides (TG) at Week 26 compared to placebo. The trial will be unblinded after study completion at Week 52 vs. Week 26 following discussions with the FDA. The primary endpoint will be analyzed after study unblinding at Week 52 to minimize any potential bias that may be introduced due to the unblinding of data prior to completion of the trial. This approach is aligned with our strategy of prioritizing MASH and filing for SHTG after MASH. Secondary endpoints include the assessment of liver fat measured by magnetic resonance imaging proton density fat fraction (MRI-PDFF), non-high-density lipoprotein cholesterol (non-HDL-C), high-density lipoprotein cholesterol (HDL-C), apolipoprotein B (apo-B), very low-density lipoprotein cholesterol (VLDL-C), HbA1c for those with baseline ≥ 6.5%, and total cholesterol (TC) at week 26 compared to placebo.

In December 2024, we completed enrollment in the ENTRUST trial with a total of 369 patients. We expect to report topline data from ENTRUST in the first quarter of 2026.

Agreements with Teva

FGF21 Agreement

In April 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 pegozafermin), 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 pegozafermin and products containing pegozafermin. 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 pegozafermin and products containing pegozafermin.

Under the FGF21 Agreement, we are obligated to use commercially reasonable efforts to develop and commercialize pegozafermin 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, we paid Teva a nonrefundable upfront payment of $6.0 million. In addition, under each agreement, we are required to pay Teva $2.5 million upon the achievement of a specified clinical development milestone (payable once, upon the first time such milestone is achieved), and additional payments totaling up to $65.0 million upon achievement of certain commercial milestones. In the fourth quarter of 2023, we made a $2.5 million milestone payment to Teva under the FGF21 Agreement following the achievement of a clinical development milestone related to our ENTRUST clinical trial in SHTG. 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 pegozafermin. 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 pegozafermin in such country, (2) the expiration of data or regulatory exclusivity for pegozafermin in such country and (3) 10 years from the first commercial sale of pegozafermin 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 pegozafermin 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.

FASN Agreement

Concurrently with the FGF21 Agreement described above, we also acquired rights to Teva patents, intellectual property and other assets relating to Teva's development program of small molecule inhibitors of Fatty Acid Synthase (the "FASN Agreement"). We did not develop any product candidates under the FASN Agreement and all rights associated with the program were returned to Teva in the fourth quarter of 2024.

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. Generally, before a new therapeutic product can be marketed, considerable data demonstrating a biological product candidate's quality, safety, purity and

potency, or a small molecule drug candidate's quality, safety and efficacy, must be obtained, organized into a format specific for each regulatory authority, submitted for review and approved by the regulatory authority. For biological product candidates, potency is similar to efficacy and is interpreted to mean the specific ability or capacity of the product, as indicated by appropriate laboratory tests or by adequately controlled clinical data obtained through the administration of the product in the manner intended, to effect a given result.

Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or post-marketing may subject an applicant to administrative or judicial sanctions. These sanctions could include, among other actions, the FDA's refusal to approve pending applications from the sponsor, withdrawal of an approval, a clinical hold, untitled or warning letters, product recalls or market withdrawals, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement and civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on our company and our products or product candidates.

U.S. Biologics Regulation

In the United States, biological products are subject to regulation under the Federal Food, Drug, and Cosmetic Act ("FDCA"), the Public Health Service Act ("PHSA") and other federal, state, local, and foreign statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, and local statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or following approval may subject an applicant to administrative action and judicial sanctions. 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 Practices ("GLP") regulation;
- submission to the FDA of an IND, which must become effective before clinical trials may begin and must be updated annually or when significant changes are made;
- approval by an independent institutional review board ("IRB"), or ethics committee at each clinical site before the trial is commenced;
- manufacture of the proposed biologic candidate in accordance with current Good Manufacturing Practices "(cGMP");
- performance of adequate and well-controlled human clinical trials in accordance with Good Clinical Practice ("GCP") requirements to establish the safety, purity and potency of the proposed biologic product candidate for its intended purpose;
- preparation of and submission to the FDA of a BLA, after completion of all pivotal clinical trials;
- 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 GCP; and
- FDA review and approval of a BLA to permit commercial marketing of the product for particular indications for use in the United States.

Preclinical and Clinical Development

Prior to beginning any clinical trial with a product candidate in the United States, we must submit an investigational new drug ("IND") application 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 on the general

investigational plan and the protocol or protocols for preclinical studies and clinical trials. The IND also includes results of animal and in vitro studies assessing the toxicology, pharmacokinetics, pharmacology and pharmacodynamic characteristics of the product, chemistry, manufacturing and controls information, and any available human data or literature to support the use of the investigational product. An IND must become effective before human clinical trials may begin. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day 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.

In addition to the IND submission process, supervision of human gene transfer trials includes evaluation and assessment by an institutional biosafety committee ("IBC"), a local institutional committee that reviews and oversees research utilizing recombinant or synthetic nucleic acid molecules at that institution. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment and such review may result in some delay before initiation of a clinical trial.

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP, which include the requirement that all research subjects provide their informed consent for their participation in any clinical 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 preclinical studies and clinical trials 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.

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all IND requirements must be met unless waived. When the foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain FDA regulatory requirements in order to use the study as support for an IND or application for marketing approval or licensure, including that the study was conducted in accordance with GCP, including review and approval by an independent ethics committee and use of proper procedures for obtaining informed consent from subjects, and the FDA is able to validate the data from the study through an onsite inspection if the FDA deems such inspection necessary. The GCP requirements encompass both ethical and data integrity standards for clinical studies.

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 studies and clinical trials, 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. Data can come from company-sponsored clinical studies intended to test the safety and effectiveness of the product, or from a number of alternative sources, including studies initiated and sponsored by investigators. The submission of a BLA requires payment of a substantial application user fee to the FDA, unless a waiver or exemption applies.

Within 60 days following submission of the application, the FDA reviews a BLA submitted to determine if it is substantially complete before the agency accepts it for filing. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In this event, the BLA must be resubmitted with the additional information. Once a BLA has been accepted for filing, the FDA's goal is to review standard applications within ten months after the filing date, 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 may also be 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. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. 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 GCP. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

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

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

A product intended to treat a serious or life-threatening disease or condition may also be eligible for Breakthrough Therapy designation to expedite its development and review. A product can receive Breakthrough Therapy designation if preliminary clinical evidence indicates that the product, alone or in combination with one or more other drugs or biologics, may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation includes all of the fast track program features, as well as more intensive FDA interaction and guidance beginning as early as Phase 1 and an organizational commitment to expedite the development and review of the product, including involvement of senior managers.

Additionally, products studied for their safety and effectiveness in treating serious or life-threatening diseases or conditions may receive accelerated approval upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of accelerated approval, the FDA will generally require the sponsor to perform adequate and well-controlled post-marketing clinical studies to verify and describe the anticipated effect on irreversible morbidity or mortality or other clinical benefit. Under the Food and Drug Omnibus Reform Act of 2022, the FDA may require, as appropriate, that such studies be underway prior to approval or within a specific time period after the date of approval for a product granted accelerated approval. Products receiving accelerated approval may be subject to expedited withdrawal procedures if the sponsor fails to conduct the required post-marketing studies or if such studies fail to verify the predicted clinical benefit. In addition, the FDA currently requires as a condition for accelerated approval, pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

Regulation of Combination Products

Certain therapeutic products are comprised of multiple components, such as drug components, biologic components, and device components, that would normally be subject to different regulatory frameworks by the FDA and frequently regulated by different centers at the FDA. These products are known as combination products. Under the FDCA, the FDA is charged with assigning a center with primary jurisdiction, or a lead center, for review of a combination product. The determination of which center will be the lead center is based on the "primary mode of action" of the combination product. Thus, if the primary mode of action of a drug/biologic-device combination product is attributable to the drug or biological product, the FDA center responsible for premarket review of the drug or biological product would have primary jurisdiction for the combination product. The FDA has also established

the Office of Combination Products to address issues surrounding combination products and provide more certainty to the regulatory review process. That office serves as a focal point for combination product issues for agency reviewers and industry. It is also responsible for developing guidance and regulations to clarify the regulation of combination products, and for assignment of the FDA center that has primary jurisdiction for review of combination products where the jurisdiction is unclear or in dispute. A combination product with a primary mode of action attributable to the drug or biologic component generally would be reviewed and approved pursuant to the drug or biologic approval processes set forth in the FDCA. In reviewing the new drug application or BLA for such a product, however, FDA reviewers would consult with their counterparts in the FDA's Center for Devices and Radiological Health to ensure that the device component of the combination product met applicable requirements regarding safety, effectiveness, durability and performance. In addition, under FDA regulations, combination products are subject to cGMP requirements applicable to both drugs and devices, including the Quality System Regulation applicable to medical devices.

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. As part of the manufacturing process, the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. After a BLA is approved for a biological product, the product also may be subject to official lot release. If the product is subject to official lot release by the FDA, the manufacturer submits samples of each lot of product to the FDA together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot. The FDA also may perform certain confirmatory tests on lots of some products before releasing the lots for distribution by the manufacturer. In addition, the FDA conducts laboratory research related to the regulatory standards on the safety, purity, and potency or effectiveness of biologics. 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 the 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;
- consent decrees, corporate integrity agreements, debarment or exclusion from federal healthcare programs;

- mandated modification of promotional materials and labeling and the issuance of corrective information;
- the issuance of safety alerts, Dear Healthcare Provider letters, press releases and other communications containing warnings or other safety information about the product; 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 (collectively, the "ACA") includes a provision called the Biologics Price Competition and Innovation Act of 2009 ("BPCIA"), which created an abbreviated approval pathway for biological products that are highly similar, or "biosimilar" to or interchangeable with an FDA-approved reference biological product. 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, is generally 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. A product shown to be biosimilar or interchangeable with an FDA-approved reference biological product may rely in part on the FDA's previous determination of safety and effectiveness for the reference product for approval, which can potentially reduce the cost and time required to obtain approval to market the product. 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.

The FDA has issued guidance documents intended to inform prospective applicants and facilitate the development of proposed biosimilars and interchangeable biosimilars, as well as to describe the FDA's interpretation of certain statutory requirements added by the BPCIA.

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.

A reference biologic is granted twelve years of exclusivity from the time of first licensure of the reference product. The first biologic product submitted under the abbreviated approval pathway that is determined to be interchangeable with the reference product has exclusivity against other biologics submitted under the abbreviated approval pathway for the lesser of (i) one year after the first commercial marketing, (ii) 18 months after approval if there is no legal challenge, (iii) 18 months after the resolution in the applicant's favor of a lawsuit challenging the biologics' patents if an application has been submitted, or (iv) 42 months after the application has been approved if a lawsuit is ongoing within the 42-month period.

The BPCIA is complex and continues to be interpreted and implemented by the FDA. In July 2018, the FDA announced an action plan to encourage the development and efficient review of biosimilars, including the establishment of a new office within the agency that will focus on therapeutic biologics and biosimilars. On December 20, 2020, Congress amended the PHSA as part of the COVID-19 relief bill to further simplify the biosimilar review process by making it optional to show that conditions of use proposed in labeling have been previously approved for the reference product, which used to be a requirement of the application. In addition, 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.

As discussed below, the Inflation Reduction Act of 2022 ("IRA") is a significant law that intends to foster generic and biosimilar competition and to lower drug and biologic costs.

Patent Term Extension

In the U.S., after a BLA is approved, owners of relevant drug patents may apply for up to a five-year patent extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory process. The allowable patent term extension is typically calculated as one-half the time between, the latter of the effective date of an IND and issue date of the patent for which extension is sought, and the submission date of a BLA, plus the time between the BLA submission date and the BLA approval date up to a maximum of five years. The time can be shortened if the FDA determines that the applicant did not pursue licensure with due diligence. The total patent term after the extension may not exceed 14 years from the date of product licensure. Only one patent applicable to a licensed biological product is eligible for extension and only those claims covering the product, a method for using it, or a method for manufacturing it may be extended and the application for the extension must be submitted prior to the expiration of the patent in question. However, we may not be granted an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Some, but not all, foreign jurisdictions possess patent term extension or other additional patent exclusivity mechanisms that may be more or less stringent and comprehensive than those of the U.S.

Other U.S. Healthcare Laws and Compliance Requirements

Pharmaceutical companies are subject to additional healthcare regulation and enforcement by the federal government and by authorities in the states and foreign jurisdictions in which they conduct their business. Such laws include, without limitation: the federal Anti-Kickback Statute ("AKS"), the federal False Claims Act ("FCA"), the Health Insurance Portability and Accountability Act of 1996 ("HIPAA") and similar foreign, federal and state fraud, abuse and transparency laws.

The AKS prohibits, among other things, persons and entities from knowingly and willfully soliciting, receiving, offering or paying remuneration, to induce, or in return for, either the referral of an individual, or the purchase or recommendation of an item or service for which payment may be made under any federal healthcare program. The term remuneration has been interpreted broadly to include anything of value. The AKS has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand, and prescribers and purchasers on the other. The government often takes the position that to violate the AKS, only one purpose of the remuneration need be to induce referrals, even if there are other legitimate purposes for the remuneration. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from AKS prosecution, but they are drawn narrowly and practices that involve remuneration, such as consulting agreements, 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. Our practices may not in all cases meet all of the criteria for

protection under a statutory exception or regulatory 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 AKS. 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. 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.

Civil and criminal false claims laws, including the FCA, and civil monetary penalty laws, which can be enforced through civil whistleblower or qui tam actions prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment of federal government funds, including in federal healthcare programs, that are false or fraudulent. Pharmaceutical and other healthcare companies have been prosecuted under these laws for engaging in a variety of different types of conduct that caused the submission of false claims to federal healthcare programs. Under the AKS, for example, a claim resulting from a violation of the AKS is deemed to be a false or fraudulent claim for purposes of the FCA.

HIPAA created additional federal criminal statutes that prohibit, among other things, executing a scheme to defraud any healthcare benefit program, including private third-party payors, and making false statements relating to healthcare matters. A person or entity does not need to have actual knowledge of the healthcare fraud statute implemented under HIPAA or specific intent to violate the statute in order to have committed a violation.

The FDCA addresses, among other things, the design, production, labeling, promotion, manufacturing, and testing of drugs, biologics and medical devices, and prohibits such acts as the introduction into interstate commerce of adulterated or misbranded drugs or devices. The PHSA also prohibits the introduction into interstate commerce of unlicensed or mislabeled biological products.

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.

The U.S. federal Physician Payments Sunshine Act requires certain manufacturers of 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 annually report to the Centers for Medicaid & Medicare Services ("CMS") information related to payments or other transfers of value to various healthcare professionals including physicians, physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, certified nurse-midwives and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Beginning on January 1, 2023, California Assembly Bill 1278 requires California physicians and surgeons to notify patients of the Open Payments database established under the federal Physician Payments Sunshine Act.

We are also subject to federal price reporting laws and federal consumer protection and unfair competition laws. Federal price reporting laws require manufacturers to calculate and report complex pricing metrics to government programs, where such reported prices may be used in the calculation of reimbursement and/or discounts on approved products. Federal consumer protection and unfair competition laws broadly regulate marketplace activities and activities that potentially harm consumers.

Ensuring business arrangements with third parties comply with applicable healthcare laws and regulations is a difficult and 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.

Data Privacy and Security

Numerous state, federal and foreign laws, govern the collection, dissemination, use, access to, confidentiality and security of personal information, including health-related information. In the United States, numerous federal and state laws and regulations, including state data breach notification laws, state health information privacy laws, and federal and state consumer protection laws and regulations, govern the collection, use, disclosure, and protection of health-related and other personal information could apply to our operations or the operations of our partners.

For example, HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 ("HITECH Act"), and their respective implementing regulations imposes data privacy, security and breach notification obligations on certain health care providers, health plans, and health care clearinghouses, known as covered entities, as well as their business associates and their covered subcontractors that perform certain services that involve using, disclosing, creating, receiving, maintaining, or transmitting individually identifiable protected health information ("PHI") for or on behalf of such covered entities.

These requirements imposed by HIPAA and the HITECH Act on covered entities and business associates include, entering into agreements that require business associates protect PHI provided by the covered entity against improper use or disclosure, among other things; following certain standards for the privacy of PHI, which limit the disclosure of a patient's past, present, or future physical or mental health or condition or information about a patient's receipt of healthcare if the information identifies, or could reasonably be used to identify, the individual; ensuring the confidentiality, integrity, and availability of all PHI created, received, maintained, or transmitted in electronic form, to identify and protect against reasonably anticipated threats or impermissible uses or disclosures to the security and integrity of such PHI; and reporting of breaches of PHI to individuals and regulators.

Entities that are found to be in violation of HIPAA may be subject to significant civil, criminal, and administrative fines and penalties and/or additional reporting and oversight obligations if required to enter into a resolution agreement and corrective action plan with HHS to settle allegations of HIPAA non-compliance. A covered entity or business associate is also liable for civil money penalties for a violation that is based on an act or omission of any of its agents, which may include a downstream business associate, as determined according to the federal common law of agency. HITECH also increased the civil and criminal penalties applicable to covered entities and 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. To the extent that we submit electronic healthcare claims and payment transactions that do not comply with the electronic data transmission standards established under HIPAA and HITECH, payments to us may be delayed or denied.

In addition, state health information privacy laws, such as California's Confidentiality of Medical Information Act and Washington's My Health My Data Act, govern the privacy and security of health-related information, specifically, may apply even when HIPAA does not and impose additional requirements.

Even when HIPAA and state health information privacy laws do not apply, according to the FTC and state Attorneys General, violating consumers' privacy rights or failing to take appropriate steps to keep consumers' personal information secure may constitute unfair acts or practices in or affecting commerce in violation of Section 5(a) of the Federal Trade Commission Act and state consumer protection laws.

In addition, certain state laws, such as the California Consumer Privacy Act of 2018 ("CCPA"), as amended by the California Privacy Rights Act of 2020 ("CPRA"), govern the privacy and security of personal information, including health-related information in certain circumstances, some of which are more stringent than HIPAA in various ways. Numerous other states have passed similar laws, but many differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts. The CCPA/CPRA applies to personal data of consumers, business representatives, and employees, and imposes obligations on certain businesses that do business in California, including to provide specific disclosures in privacy notices, and affords rights to California residents in relation to their personal information. Health information falls under the CCPA/CPRA's definition of personal information where it identifies, relates to, describes, or is reasonably capable of being associated with or could reasonably be linked, directly or indirectly, with a particular consumer or household—unless it is subject to HIPAA—and is included under a new category of personal information, "sensitive personal information," which is offered greater protection. The numerous other comprehensive privacy laws that have passed or are being considered in other states, as well as at the federal and local levels, also exempt some data processed in the context

of clinical trials; but others exempt covered entities and business associates subject to HIPAA altogether, further complicating compliance efforts, and increasing legal risk and compliance costs for us and the third parties upon whom we rely.

Additionally, our use of artificial intelligence and machine learning may be subject to laws and evolving regulations regarding the use of artificial intelligence and machine learning, controlling for data bias, and antidiscrimination.

Failure to comply with these laws, where applicable, can result in the imposition of significant civil and/or criminal penalties and private litigation. Privacy and security laws, regulations, and other obligations are constantly evolving, may conflict with each other to complicate compliance efforts, and can result in investigations, proceedings, or actions that lead to significant civil and/or criminal penalties and restrictions on data processing.

Coverage, Pricing and Reimbursement

In the United States and markets in other countries, patients generally rely on third-party payors to reimburse all or part of the costs associated with their treatment. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance. Our ability to successfully commercialize our product candidates 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. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow it to establish or maintain pricing sufficient to realize a sufficient return on its investment. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels.

Significant uncertainty exists as to the coverage and reimbursement status of any pharmaceutical or biological product for which we may obtain regulatory approval. Sales of any product, if approved, depend, in part, on the extent to which such product will be covered by third-party payors, such as federal, state, and foreign government healthcare programs, commercial insurance and managed healthcare organizations, and the level of reimbursement, if any, for such product by third-party payors. Decisions regarding whether to cover any of our product candidates, if approved, the extent of coverage and amount of reimbursement to be provided are made on a plan-by-plan basis. Further, no uniform policy for coverage and reimbursement exists in the United States, and coverage and reimbursement can differ significantly from payor to payor. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement rates, but also have their own methods and approval process apart from Medicare determinations. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our product candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance. Factors payors consider in determining reimbursement are based on whether the product is:

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

Third-party payors are increasingly challenging the prices charged for medical products and services, examining the medical necessity and reviewing the cost effectiveness of pharmaceutical or biological products, medical devices and medical services, in addition to questioning safety and efficacy. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit sales of any product that receives approval. Decreases in third-party reimbursement for any product or a decision by a third-party not to cover a product could reduce physician usage and patient demand for the product.

For products administered under the supervision of a physician, obtaining coverage and adequate reimbursement may be particularly difficult because of the higher prices often associated with such drugs. Additionally, separate reimbursement for the product itself or the treatment or procedure in which the product is

used may not be available, which may impact physician utilization. In addition, companion diagnostic tests require coverage and reimbursement separate and apart from the coverage and reimbursement for their companion pharmaceutical or biological products. Similar challenges to obtaining coverage and reimbursement, applicable to pharmaceutical or biological products, will apply to companion diagnostics.

In addition, the U.S. government, state legislatures and foreign governments have continued implementing cost-containment programs, including price controls, restrictions on coverage and reimbursement and requirements for substitution of generic products. The IRA provides CMS with significant new authorities intended to curb drug costs and to encourage market competition. For the first time, CMS will be able to directly negotiate prescription drug prices and to cap out-of-pocket costs. Each year, CMS will select and negotiate a preset number of high-spend drugs and biologics that are covered under Medicare Part B and Part D that do not have generic or biosimilar competition. On August 29, 2023, HHS announced the list of the first ten drugs subject to price negotiations. These price negotiations occurred in 2024. In January 2025, CMS announced a list of fifteen additional Medicare Part D drugs that will be subject to price negotiations. The IRA also provides a new "inflation rebate" covering Medicare patients that took effect in 2023 and is intended to counter certain price increases in prescriptions drugs. The inflation rebate provision requires drug manufacturers to pay a rebate to the federal government if the price for a drug or biologic under Medicare Part B and Part D increases faster than the rate of inflation. To support biosimilar competition, beginning in October 2022, qualifying biosimilars may receive a Medicare Part B payment increase for a period of five years. Separately, if a biologic drug for which no biosimilar exists delays a biosimilar's market entry beyond two years, CMS will be authorized to subject the biologics manufacturer to price negotiations intended to ensure fair competition. Notwithstanding these provisions, the IRA's impact on commercialization and competition remains largely uncertain.

In addition, 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. 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 reimbursement will be available for any product candidate that we may commercialize and, if reimbursement is available, the level of reimbursement. In addition, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average sales price, or ASP, and best price. Penalties may apply in some cases when such metrics are not submitted accurately and timely. Further, these prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs.

Finally, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. 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. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our product candidates. Historically, products launched in the European Union do not follow price structures of the U.S. and generally prices tend to be significantly lower.

Healthcare Reform

The United States and some foreign jurisdictions are considering or have enacted a number of reform proposals to change the healthcare system. There is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by federal and state legislative initiatives, including those designed to limit the pricing, coverage, and reimbursement of pharmaceutical and biopharmaceutical products, especially under government-funded health care programs, and increased governmental control of drug pricing.

The ACA, which was enacted in March 2010, substantially changed the way healthcare is financed by both governmental and private insurers in the United States, and significantly affected the pharmaceutical industry. The ACA contains a number of provisions of particular import to the pharmaceutical and biotechnology industries, including, but not limited to, those governing enrollment in federal healthcare programs, a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, and annual fees based on pharmaceutical companies' share of sales to federal health care programs. Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. For example, the IRA, among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA also eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost and creating a new manufacturer discount program.

Other legislative changes have been proposed and adopted since the ACA was enacted, including automatic aggregate reductions of Medicare payments to providers of on average 2% per fiscal year as part of the federal budget sequestration under the Budget Control Act of 2011. These reductions went into effect in April 2013 and, due to subsequent legislative amendments, will remain in effect until 2032 unless additional action is taken by Congress. In addition, the Bipartisan Budget Act of 2018, among other things, amended the Medicare Act (as amended by the ACA) to increase the point-of-sale discounts that manufacturers must agree to offer under the Medicare Part D coverage discount program from 50% to 70% off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs being covered under Medicare Part D.

Moreover, there has recently been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state measures designed to, among other things, reduce the cost of prescription drugs, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. For example, in May 2019, CMS adopted a final rule allowing Medicare Advantage Plans the option to use step therapy for Part B drugs, permitting Medicare Part D plans to apply certain utilization controls to new starts of five of the six protected class drugs, and requiring the Explanation of Benefits for Part D beneficiaries to disclose drug price increases and lower cost therapeutic alternatives, which went into effect on January 1, 2021. In response to the Biden administration's October 2022 executive order, on February 14, 2023, HHS released a report outlining three new models for testing by the CMS Innovation Center which will be evaluated on their ability to lower the cost of drugs, promote accessibility, and improve quality of care. It is unclear whether the models will be utilized in any health reform measures in the future. Further, on December 7, 2023, the Biden administration announced an initiative to control the price of prescription drugs through the use of march-in rights under the Bayh-Dole Act. On December 8, 2023, the National Institute of Standards and Technology published for comment a Draft Interagency Guidance Framework for Considering the Exercise of March-In Rights which for the first time includes the price of a product as one factor an agency can use when deciding to exercise march-in rights. While march-in rights have not previously been exercised, it is uncertain if that will continue under the new framework. Notwithstanding the IRA, continued legislative and enforcement interest exist in the United States with respect to specialty drug pricing practices. Specifically, we expect regulators to continue pushing for transparency to drug pricing, reducing the cost of prescription drugs under Medicare, reviewing the relationship between pricing and manufacturer patient programs, and reforming government program reimbursement methodologies for drugs.

Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain drug access and marketing cost disclosure and transparency measures, and designed to encourage importation from other countries and bulk purchasing. Legally mandated price controls on payment amounts by third-party payors or other restrictions could harm our business, financial condition, results of operations and prospects. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. This could reduce the ultimate demand for its drugs or put pressure on its drug pricing, which could negatively affect our business, financial condition, results of operations and prospects.

Drug and Biologic Development Process in the European Union

The conduct of clinical trials in the EU is governed by the EU Clinical Trials Regulation (EU) No. 536/2014 ("CTR") which entered into force on January 31, 2022. Under the CTR, a sponsor will be able to submit a single application for approval of a clinical trial through a centralized EU clinical trials portal, called the Clinical Trials Information System or CTIS. One national regulatory authority (the reporting EU Member State proposed by the applicant) will take the lead in validating and evaluating the application consult and coordinate with the other concerned member states. If an application is rejected, it may be amended and resubmitted through the EU clinical trials portal. If an approval is issued, the sponsor may start the clinical trial in all concerned member states. However, a concerned EU Member State may in limited circumstances declare an "opt-out" from an approval and prevent the clinical trial from being conducted in such member state. The CTR also aims to streamline and simplify the rules on safety reporting, and introduces enhanced transparency requirements such as mandatory submission of a summary of the clinical trial results to the EU Database. The CTR foresees a three-year transition period. EU Member States will work in CTIS immediately after the system has gone live. Since January 31, 2023, submission of initial clinical trial applications via CTIS is mandatory and CTIS serves as the single entry point for submission of clinical trial-related information and data. By January 31, 2025, all ongoing trials approved under the former Clinical Trials Directive will need to comply with the CTR and have to be transitioned to CTIS. On July 19, 2023, the European Committee (the "EC") published guidance concerning the steps to be taken in this transition. This guidance provides, among other things, that (i) documentation which was previously assessed will not be reassessed, (ii) templates that were developed and endorsed by the EU Clinical Trials Expert Group to provide compliance with the CTR do not need to be updated and (iii) there is no need to retrospectively create a site suitability form, which are only necessary for new trial sites. Under both the former regime and the new CTR, national laws, regulations and the applicable GCP and Good Laboratory Practice standards must also be respected during the conduct of the trials, including the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use guidelines on Good Clinical Practice and the ethical principles that have their origin in the Declaration of Helsinki.

During the development of a medicinal product, the EMA and national regulators within the EU provide the opportunity for dialogue and guidance on the development program. At the EMA level, this is usually done in the form of scientific advice, which is given by the Committee for Medicinal Products for Human Use ("CHMP") on the recommendation of the Scientific Advice Working Party. A fee is incurred with each scientific advice procedure, but is significantly reduced for designated orphan medicines. Advice from the EMA is typically provided based on questions concerning, for example, quality (chemistry, manufacturing and controls testing), nonclinical testing and clinical studies, and pharmacovigilance plans and risk-management programs. Advice is not legally binding with regard to any future Marketing Authorization Application ("MAA") of the product concerned.

Drug Marketing Authorization in the European Union

In the EU and in Iceland, Norway and Liechtenstein (together the European Economic Area or "EEA"), after completion of all required clinical testing, pharmaceutical products may only be placed on the market after obtaining a Marketing Authorization ("MA"). To obtain an MA of a drug under European Union regulatory systems, an applicant can submit an MAA through, amongst others, a centralized or decentralized procedure.

Centralized Authorization Procedure

The centralized procedure provides for the grant of a single MA that is issued by the EC following the scientific assessment of the application by the EMA that is valid for all EU Member States as well as in the three additional EEA Member States (Norway, Iceland and Liechtenstein). The centralized procedure is compulsory for specific medicinal products, including for medicines developed by means of certain biotechnological processes, products designated as orphan medicinal products, advanced therapy medicinal products (gene therapy, somatic cell therapy, or tissue engineered medicines) and medicinal products with a new active substance indicated for the treatment of certain diseases (HIV/AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases). For medicinal products containing a new active substance not yet authorized in the EEA before May 20, 2004 and indicated for the treatment of other diseases, medicinal products that constitute significant therapeutic, scientific or technical innovations or for which the grant of a MA through the centralized procedure would be in the interest of public health at EU level, an applicant may voluntarily submit an application for a MA through the centralized procedure.

Under the centralized procedure, the CHMP, established at the EMA, is responsible for conducting the initial assessment of a drug. The CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing MA. Under the centralized procedure, the timeframe for the evaluation of an MAA by the EMA's CHMP is, in principle, 210 days from receipt of a valid MAA. However, this timeline excludes clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the CHMP, so the overall process typically takes a year or more, unless the application is eligible for an accelerated assessment. Accelerated evaluation might be granted by the CHMP in exceptional cases when a medicinal product is expected to be of major public health interest, particularly from the point of view of therapeutic innovation. Upon request, the CHMP can reduce the time frame to 150 days if the applicant provides sufficient justification for an accelerated assessment. The CHMP will provide a positive opinion regarding the application only if it meets certain quality, safety and efficacy requirements. This opinion is then transmitted to the EC, which has the ultimate authority for granting MA within 67 days after receipt of the CHMP opinion.

Decentralized Authorization Procedure

The decentralized procedure permits companies to file identical MA applications for a medicinal product to the competent authorities in various EU Member States simultaneously if such medicinal product has not received marketing approval in any EU Member State before. This procedure is available for pharmaceutical products not falling within the mandatory scope of the centralized procedure. The competent authority of a single EU Member State, known as the reference member state, is appointed to review the application and provide an assessment report. The competent authorities of the other EU Member States, the concerned member states, are subsequently required to grant a MA for their territories on the basis of this assessment. The only exception to this is where the competent authority of an EU Member State considers that there are concerns of potential serious risk to public health, the disputed points are subject to a dispute resolution mechanism and may eventually be referred to the EC, whose decision is binding for all EU Member States.

Risk Management Plan

All new MAAs must include a Risk Management Plan ("RMP"), describing the risk management system that the company will put in place and documenting measures to prevent or minimize the risks associated with the product. RMPs are continually modified and updated throughout the lifetime of the medicine as new information becomes available. An updated RMP must be submitted (i) at the request of EMA or a national competent authority, or (ii) whenever the risk-management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit-risk profile or as a result of an important pharmacovigilance or risk-minimization milestone being reached. The regulatory authorities may also impose specific obligations as a condition of the MA. Since October 20, 2023, all RMPs for centrally authorized products are published by the EMA subject only to limited redactions.

MA Validity Period

MAs have an initial duration of five years. After these five years, the authorization may subsequently be renewed on the basis of a reevaluation of the risk-benefit balance. Once renewed, the MA is valid for an unlimited period unless the EC or the national competent authority decides, on justified grounds relating to pharmacovigilance, to proceed with only one additional five-year renewal. Applications for renewal must be made to the EMA at least nine months before the five-year period expires.

Data and Market Exclusivity in the European Union

As in the United States, it may be possible to obtain a period of market and/-or data exclusivity in the EU that would have the effect of postponing the entry into the marketplace of a competitor's generic, hybrid or biosimilar product (even if the pharmaceutical product has already received a MA) and prohibiting another applicant from relying on the MA holder's pharmacological, toxicological and clinical data in support of another MA for the purposes of submitting an application, obtaining MA or placing the product on the market. Innovative medicinal products, referred to as New Chemical Entities ("NCE") approved in the EU qualify for eight years of data exclusivity and 10 years of marketing exclusivity.

An additional non-cumulative one-year period of marketing exclusivity is possible if during the data exclusivity period (the first eight years of the 10-year marketing exclusivity period), the MA holder obtains an

authorization for one or more new therapeutic indications that are deemed to bring a significant clinical benefit compared to existing therapies.

The data exclusivity period begins on the date of the product's first MA in the EU. After eight years, a generic product application may be submitted and generic companies may rely on the MA holder's data. However, a generic product cannot launch until two years later (or a total of 10 years after the first MA in the EU of the innovator product), or three years later (or a total of 11 years after the first MA in the EU of the innovator product) if the MA holder obtains MA for a new indication with significant clinical benefit within the eight-year data exclusivity period. Additionally, another noncumulative one-year period of data exclusivity can be added to the eight years of data exclusivity where an application is made for a new indication for a well-established substance, provided that significant pre-clinical or clinical studies were carried out in relation to the new indication. Another year of data exclusivity may be added to the eight years, where a change of classification of a pharmaceutical product has been authorized on the basis of significant pre-trial tests or clinical trials (when examining an application by another applicant for or holder of market authorization for a change of classification of the same substance the competent authority will not refer to the results of those tests or trials for one year after the initial change was authorized).

Products may not be granted data exclusivity since there is no guarantee that a product will be considered by the European Union's regulatory authorities to include a NCE. Even if a compound is considered to be a NCE and the MA applicant is able to gain the prescribed period of data exclusivity, another company nevertheless could also market another version of the medicinal product if such company can complete a full MAA with their own complete database of pharmaceutical tests, preclinical studies and clinical trials and obtain MA of its product.

On April 26, 2023, the EC submitted a proposal for the reform of the European pharmaceutical legislation. The current draft envisages e.g., a shortening of the periods of data exclusivity, however, there is currently neither a final version of this draft nor a date for its entry into force. While the European Parliament adopted its approving position on the reform on April 10, 2024, no further required legislative steps have been taken since.

European Data Laws

The collection and use of personal health data and other personal data in the EU is governed by the provisions of the European General Data Protection Regulation (EU) 2016/679 ("GDPR"), which came into force in May 2018, and related data protection laws in individual EU Member States.

The GDPR imposes a number of strict obligations and restrictions on the ability to process, including collecting, analyzing and transferring, personal data of individuals, in particular with respect to health data from clinical trials and adverse event reporting. The GDPR includes requirements relating to the legal basis of the processing (such as consent of the individuals to whom the personal data relates), the information provided to the individuals prior to processing their personal data, the personal data breaches which may have to be notified to the national data protection authorities and data subjects, the measures to be taken when engaging processors, and the security and confidentiality of the personal data. EU Member States may also impose additional requirements in relation to health, genetic and biometric data through their national legislation.

In addition, the GDPR imposes specific restrictions on the transfer of personal data to countries outside of the EEA that are not considered by the EC to provide an adequate level of data protection. Appropriate safeguards are required to enable such transfers. Among the appropriate safeguards that can be used, the data exporter may use the standard contractual clauses ("SCCs"). When relying on SCCs, data exporters are also required to conduct a transfer risk assessment to verify if anything in the law and/or practices of the third country may impinge on the effectiveness of the SCCs in the context of the transfer at stake and, if so, to identify and adopt supplementary measures that are necessary to bring the level of protection of the data transferred to the EU standard of essential equivalence. Where no supplementary measure is suitable, the data exporter should avoid, suspend or terminate the transfer. With regard to the transfer of data from the EEA to the United States, on July 10, 2023, the EC adopted its adequacy decision for the EU-US Data Privacy Framework. On the basis of the new adequacy decision, personal data can flow from the EEA to U.S. companies participating in the framework. With regard to the transfer of data from the EU to the United Kingdom (UK), personal data may freely flow from the EEA to the UK since the UK is deemed to have an adequate data protection level. However, the adequacy decisions include a 'sunset clause' which entails that the decisions will automatically expire four years after their entry into force, unless renewed.

Failure to comply with the requirements of the GDPR and the related national data protection laws of the EU Member States may result in significant monetary fines for noncompliance of up to €20 million or 4% of the annual global revenues of the noncompliant company, whichever is greater, other administrative penalties and a number of criminal offenses for organizations and, in certain cases, their directors and officers, as well as civil liability claims from individuals whose personal data was processed. Data protection authorities from the different EU Member States may still implement certain variations, enforce the GDPR and national data protection laws differently, and introduce additional national regulations and guidelines, which adds to the complexity of processing personal data in the EU.

Furthermore, there are specific requirements relating to processing health data from clinical trials, including public disclosure obligations provided in the EU Clinical Trials Regulation No. 536/2014 (CTR), EMA disclosure initiatives and voluntary commitments by industry. Failure to comply with these obligations could lead to government enforcement actions and significant penalties against us, harm to our reputation, and adversely impact our business and operating results.

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 pegozafermin 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 MASH, 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 MASH, will increase.

If pegozafermin is approved for the treatment of MASH, future competition could also arise from select products that have been approved for MASH or currently in development, including, but not limited to: resmetirom, an approved therapy for F2-F3 MASH, which is a thyroid hormone receptor beta agonist from Madrigal Pharmaceuticals, Inc.; semaglutide, a GLP-1 receptor agonist from Novo Nordisk A/S; efruxifermin, an FGF21 analog from Akero Therapeutics, Inc.; lanifibranor, a pan-peroxisome proliferator-activated receptor alpha/delta/gamma agonist from Inventiva; survodutide, a glucagon/GLP-1 receptor dual agonist from Boehringer Ingelheim; denifanstat, a selective Fatty Acid Synthase inhibitor from Sagimet Biosciences Inc.; zalfermin/NNC0194-0499, an FGF21 analog from Novo Nordisk; and efimosfermin alfa/BOS-580, an FGF21 analog from Boston Pharmaceuticals.

If pegozafermin is approved for the treatment of SHTG, we would face competition from currently approved and marketed products, including, but not limited to, statins, fibrates, Vascepa®, a pure eicosapentaenoic acid (EPA) from Amarin Corp, and Lovaza®, an EPA and docosahexaenoic acid from GlaxoSmithKline, as well as generic products. Further competition could arise from products currently in development, including: olezarsen/AKCEA-APOCIII-LRx, an APOC3 inhibitor from Ionis; and plozasiran, an ApoC-III inhibitor 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 pegozafermin, 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 pegozafermin or any future product candidate receives marketing approval.

Pegozafermin 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.

We have established supply agreements with Northway Biotechpharma ("BTPH") and BiBo Biopharma Engineering Co., Ltd. ("BiBo") for the supply of pegozafermin for our ongoing clinical trials. Furthermore, we are collaborating with BiBo on process optimization to facilitate large-scale production for future clinical trials and potential commercialization. As part of this collaboration, we have successfully completed a large-scale GMP production run of pegozafermin, demonstrating the scalability of our manufacturing process.

We have successfully developed two refrigerated liquid formulations. These formulations are approved by the FDA and are currently in use in our trials. In addition, we have entered into a contract with two commercial fill vendors. We may in the future develop an autoinjector to deliver the liquid formulations.

Manufacturing Development Agreements

In April 2024, we entered into a collaboration agreement (the "Collaboration Agreement") with BiBo, pursuant to which BiBo will construct a production facility specifically designed to supply us with pegozafermin for commercialization, if approved (the "Production Facility"). Pursuant to the Collaboration Agreement, BiBo will build the Production Facility at BiBo's facility in the Lin-gang Special Area of China (Shanghai) Pilot Free Trade Zone to manufacture the bulk active ingredient (the "Drug Substance") required to produce pegozafermin for commercial supply. The platform is expected to provide us with manufacturing capacity to meet our commercial needs.

In May 2018, we entered into a master services agreement with BTPH, pursuant to which BTPH will provide us certain services, including development, manufacturing, and storing of pegozafermin, under statements of work for such services to be agreed by the parties from time to time.

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 ten families:

The first family is entitled “Remodeling and GlycoPEGylation of Fibroblast Growth Factor (FGF).” This patent family provides granted patent protection in 39 countries around the globe, including the United States (U.S. Patent Number 9,200,049, expiry date: June 25, 2028; and U.S. Patent Number 10,874,714, expiry date: October 10, 2028), Canada, Europe (broadly), and Japan (all 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 pegozafermin and pharmaceutical compositions thereof, as well as methods for making and using pegozafermin to treat FGF21 deficiency in a patient in need thereof.

The second family is entitled “Mutant FGF-21 Peptide Conjugate and Uses Thereof” and is specifically directed to pegozafermin. The Patent Cooperation Treaty (“PCT”) Patent Application for this family was filed on September 4, 2018 (PCT/IB2018/001112). 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/IB2018/01112 and from which U.S. Patent Number 10,407,479 was 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 pegozafermin and a defined genus specifically encompassing pegozafermin and compositions thereof (including site-specific mutations at positions 173 and 176), as well as methods for making and using pegozafermin for a variety of therapeutic indications. Such indications include methods for treating MASH or metabolic syndrome. Pegozafermin is particularly relevant for subjects with diabetes Type 2, MASH, and metabolic syndrome who require blood glucose or HbA1C reduction. The claims encompass different therapeutic regimens for administering pegozafermin (e.g., once a week or once every two weeks), which regimens are based on pegozafermin’s long half-life in vivo. This patent family provides granted patent protection of pegozafermin in 24 ex-United States jurisdictions around the globe: Australia, Canada, China, Europe (broadly), Israel, Japan, Korea and Hong Kong (expiry date: September 4, 2038). One U.S. Patent Application and one China Patent Application are pending in this family.

The third family is entitled “Methods of Treatment Using Mutant FGF-21 Peptide Conjugates.” This patent family provides granted patent protection in the United States with claims directed to dosage regimen for treating MASH (U.S. Patent Numbers 11,427,623 and 12,037,376). The term of the U.S. Patent Number 11,427,623 and 12,037,376 is September 4, 2038. One U.S. Patent Application is pending in this family.

The fourth family is entitled “Methods for promoting weight loss.” A PCT application was filed January 29, 2021 (PCT/IB2021/000044) with claims directed towards method to reduce total body weight, body fat content and/or BMI. A United States National phase application was filed July 20, 2022 and is pending.

The fifth family is entitled “Liquid Formulations Comprising Mutant FGF-21 Peptide Pegylated Conjugates” with claims directed to stable liquid formulation of FGF21. A PCT Patent Application for this family was filed on March 10, 2022. This patent family provides granted patent protection in the United States and China with claims directed to pegozafermin liquid formulations (U.S. Patent Numbers 11,596,669 and 11,850,275). The term of the U.S. Patent Numbers 11,596,669 and 11,850,275 and China patent is March 10, 2042. One U.S. patent application is pending. This patent family also includes six patent applications in ex-United States jurisdictions (Australia, Canada, China, Europe, Israel and Japan). We will continue to file patent applications to cover various formulations of FGF21.

The sixth family is entitled “Chemical Synthesis of Cytidine-5’-Monophospho-N-Glycyl-Sialic Acid” with claims directed to the chemical synthesis of Cytidine-5’-Monophospho-N-Glycyl-Sialic Acid. A PCT Patent Application was filed on December 20, 2022. A corresponding patent application is pending in the United States, Australia, Canada, China, Europe, Israel, Korea and Japan.

The seventh family is entitled “Composition and Method of Treatment for Severe Hypertriglyceridemia.” A PCT Patent Application and a U.S. Patent Application were filed June 23, 2023. This patent family provides granted patent protection in the United States (U.S. Patent Number 12,036,284). The term of the U.S. Patent Number 12,036,284 is June 23, 2043. One U.S. patent application is pending. This patent family also includes 7 patent applications in ex-United States jurisdictions (Australia, Canada, China, Europe, Israel, Japan and Korea).

The eighth family is entitled “Methods of Treatment of NASH Using Mutant FGF-21 Peptide Conjugates.” A PCT Patent Application was filed August 24, 2023.

The ninth family is entitled “Therapeutic Regimens and Methods of Treatment of NASH Using Mutant FGF-21 Peptide Conjugates.” A PCT Patent Application was filed August 23, 2024.

The tenth family is entitled “Production of Recombinant Analog of Human FGF21 Protein.” A U.S. provisional application was filed April 12, 2024.

We expect to continue to file patent applications to cover method of treating different indications.

Human Capital Management

As of December 31, 2024, we had 93 full-time employees, of which 70 employees are engaged in research and development activities. 85 of our full-time employees are located in the United States, including at our facilities in San Francisco, California, and eight of our full-time employees are located outside of the United States. We consider our relationship with our employees to be good. We have never had a work stoppage, and none of our employees is represented by a labor organization or under any collective bargaining arrangements.

We track and report internally on key talent metrics including workforce demographics and the status of open positions. We value equality and inclusion in the workforce and are proud that different groups are represented among our employees. We work diligently to confirm that our norms, practices, and policies support our equal employment opportunity commitment. We regularly and anonymously survey employees to fully understand their experience. As of December 31, 2024, approximately 62% of our employees identify as female and 38% identify as male.

Attracting, developing and retaining talented employees to support the growth of our business is an integral part of our human capital strategy and critical to our long-term success. We continue to seek additions to our staff, although the competition in our industry and in the San Francisco area, where our headquarters is located, is significant. The principal purpose of our equity incentive and annual bonus programs is to attract, retain and motivate personnel through the granting of stock-based compensation awards and cash-based performance bonus awards. As a biopharmaceutical company, we recognize the importance of access to high quality healthcare and as

such we cover 90% of our employees' monthly healthcare premiums. We offer a package of competitive employee benefits, including 401(k) plan matching contributions and an employee stock purchase plan.

We have a performance appraisal process in which managers provide regular feedback to assist with the success and development of our employees. We also invest in the growth and development of our employees through various training and opportunities that enable employees to be more effective in their roles.

We believe our management team has the necessary experience to effectively execute our strategy to achieve our corporate goals. A large majority of our employees have obtained degrees in their professions.

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 655 Montgomery Street, Suite 1500, San Francisco, California 94111 and our telephone number is (415) 432-9270. 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 Securities and Exchange Commission ("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.

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, and new risks will emerge from time to time. It is not possible for our management to predict all risks. Moreover, some of the factors, events and contingencies discussed below may have occurred in the past, but the disclosures below are not representations as to whether or not the factors, events or contingencies have occurred in the past, and instead reflect our beliefs and opinions as to the factors, events or contingencies that could materially and adversely affect us in the future.

Risk Factor Summary

- 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.
- Our business depends on the success of pegozafermin, our only product candidate under clinical development, which has not completed a pivotal trial. If we are unable to obtain regulatory approval for and successfully commercialize pegozafermin or other future product candidates, or we experience significant delays in doing so, our business will be materially harmed.
- 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.
- 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 pegozafermin or develop new product candidates.
- If we experience delays in clinical testing, our commercial prospects will be adversely affected, our costs may increase and our business may be harmed.
- If we encounter difficulties in enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.
- We have relied on, and expect to continue to rely on, third-party manufacturers and vendors to produce and release pegozafermin or any future product candidates. Any failure by a third-party to produce and release 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.
- Pegozafermin 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.
- We are developing pegozafermin for the treatment of MASH and SHTG. The requirements for approval of pegozafermin by the FDA and comparable foreign regulatory authorities may be difficult to predict and may change over time, which makes it difficult to predict the timing and costs of the clinical development.

- 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.
- 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.
- 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.
- We face substantial competition, which may result in others discovering, developing or commercializing competing products before or more successfully than we do.
- Unstable market and economic conditions, inflation, fluctuations in interest rates, natural disasters, public health crises, political crises, geopolitical events, such as the crisis in Ukraine and Israel, or other macroeconomic conditions, may have serious adverse consequences on our business and financial condition.
- Our Loan Agreement contains certain covenants that could adversely affect our operations and, if an event of default were to occur, we could be forced to repay any outstanding indebtedness sooner than planned and possibly at a time when we do not have sufficient capital to meet this obligation.
- Pegozafermin has not received regulatory approval. If we are unable to obtain regulatory approvals to market pegozafermin or any future product candidates, our business will be adversely affected.
- Our success depends upon our ability to obtain and maintain intellectual property protection for our products and technologies.
- 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 pegozafermin. 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.

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 focused on organizing and staffing our company, raising capital, acquiring our initial product candidate, pegozafermin, and licensing certain related technology, conducting research and development activities, including preclinical studies and 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.

Pegozafermin is in development and, to date, we have not generated any revenue from the licensing or commercialization of pegozafermin. We will not be able to generate product revenue unless and until pegozafermin or any future product candidate, alone or with future partners, successfully completes clinical trials, receives regulatory approval and is successfully commercialized. As pegozafermin is in 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.

We are not profitable and have incurred net losses since our inception. 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, pegozafermin and any future product candidates. We expect to incur substantial and increasing operating losses over the next several years as our research and development, clinical trials and manufacturing activities increase. In addition, because of the numerous risks and uncertainties associated with pharmaceutical product development, including that our product candidates may not advance or may take longer than expected to advance through development or may not 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. 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. 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.

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

The primary focus of our product development is pegozafermin for the treatment of patients with MASH and the treatment of patients with SHTG. Currently, pegozafermin 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 pegozafermin for the treatment of MASH or 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 pegozafermin. If we cannot successfully develop, obtain regulatory approval for and commercialize pegozafermin, we may not be able to continue our operations. The future regulatory and commercial success of pegozafermin is subject to a number of risks, including that, if approved for MASH or SHTG, pegozafermin will likely compete with products that may reach approval for the treatment of MASH prior to pegozafermin, products that are currently approved for the treatment of SHTG and the off-label use of currently marketed products for MASH and SHTG.

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.

Pegozafermin 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 pegozafermin, may not prove to be safe and effective in clinical trials. We have limited direct experience as a company in conducting pivotal trials required to obtain regulatory approval and we expect that the Phase 3 trials we are conducting will be more expansive and complex than the trials we have conducted to date. We may be unable to conduct clinical trials at preferred sites, enlist clinical investigators, enroll sufficient numbers of participants, procure sufficient drug supply 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. We may be unable to design and execute a clinical trial to support regulatory approval. Even if an ongoing clinical trial is successful, it may be insufficient to demonstrate that pegozafermin 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 pegozafermin 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 pegozafermin 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, pegozafermin 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, Phase 1b/2a and Phase 2 clinical trials have involved small patient populations and, because of the small sample size in such trials, the results of those clinical trials may be subject to substantial variability, including the inherent variability associated with biopsies in MASH patients, and may not be indicative of either future interim results or final results in future trials of patients with liver or cardio-metabolic diseases. If we are unable to successfully demonstrate the safety and efficacy of pegozafermin or other future product candidates and receive the necessary regulatory approvals, our business will be materially harmed.

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 pegozafermin 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 in connection with our ongoing activities, particularly as we conduct Phase 3 clinical trials of, seek regulatory approval for and prepare for commercialization of pegozafermin. We believe our existing cash, cash equivalents and marketable securities, supplemented by $269.9 million in net proceeds from our February 2025 equity offering, will be sufficient to fund our projected operating requirements for a period of at least one year following the filing of this Form 10-K.

We will require additional capital to discover, develop, obtain regulatory approval for and commercialize pegozafermin and any future product candidates. Our ability to complete new and ongoing clinical trials for pegozafermin may be subject to our ability to raise additional capital. We do not have any committed external source of funds other than as a result of any sales that we may make under the 2023 ATM Facility (as defined below) and proceeds from our Loan Agreement, which are subject to the achievement of certain milestones and/or consent of the lenders. 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. The current market environment for small biotechnology companies, like 89bio, and broader macroeconomic factors may preclude us from successfully raising additional capital.

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 pegozafermin 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 rights relating to pegozafermin, and from whom we licensed patents and know-how related to glycoPEGylation technology that is used in the manufacture of pegozafermin. For additional information regarding this license agreement, please see Note 5 to our consolidated financial statements appearing under Part II, Item 8 of this Annual Report.

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

We cannot guarantee that we will be able to initiate and complete clinical trials and successfully accomplish all required regulatory activities or other activities necessary to gain approval and commercialize pegozafermin or any future product candidates. We currently have two active IND applications with the FDA in the United States for pegozafermin. In the future, we may file an additional IND with another division for any future indications or future product candidates. 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. As a result, 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 pegozafermin 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 pegozafermin or any future product candidates and may harm our business, results of operations and prospects. 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 pegozafermin 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 including, for example, a new formulation, 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 pegozafermin 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 future clinical trials, and even once enrolled, we may be unable to retain a sufficient number of patients to complete any of our trials. Furthermore, there are inherent difficulties in diagnosing MASH, which can currently only be definitively diagnosed through a liver biopsy, and identifying SHTG patients. Specifically, identifying patients most likely to meet MASH enrollment criteria on biopsy is an ongoing challenge, with existing clinical indicators lacking both sensitivity and specificity. As a result, MASH trials often suffer from high levels of screen failure following central review of the baseline liver biopsy, which can lead to lower enrollment. In addition, we do not have experience enrolling patients with cirrhosis and such enrollment make take longer than we expect. As a result of such difficulties and the significant competition for recruiting MASH and SHTG 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. 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. 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. Further, enrollment in Phase 3 clinical trials may be adversely affected by the marketing approval for Rezdiffra™ or the potential marketing approvals for one or more investigational MASH drugs if patients choose to take an approved drug rather than enroll in a clinical trial. In addition, our ability to receive accelerated approval of pegozafermin using data from the histology cohorts for non-cirrhotic (F2-F3) and cirrhotic (F4) MASH may be adversely affected if another company's product candidate receives full approval before we receive accelerated approval. 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. 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 pegozafermin and any future product candidates. We plan to leverage the safety database from the SHTG Phase 3 program across both the SHTG and MASH indications. If we are not able enroll enough patients in our trials sufficient to support the safety database, our ability to advance the development of pegozafermin may be adversely affected.

We have relied on, and expect to continue to rely on, third-party manufacturers and vendors to produce and release pegozafermin or any future product candidates. Any failure by a third-party to produce and release 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.

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 pegozafermin and any future product candidates. We currently have contractual relationships with BTPH and BiBo pursuant to which they supply us with pegozafermin for our clinical trials. If there should be any disruption in our supply arrangement with BTPH or BiBo, including any adverse events affecting either party, it could have a negative effect on the clinical development of pegozafermin if our other manufacturer is not able to produce sufficient quantities of pegozafermin and we need to qualify an alternate supply source.

We expect to continue to rely on third-party manufacturers and suppliers, including BiBo, if we receive regulatory approval for pegozafermin or any other product candidates. BiBo is constructing a production facility in China specifically designed to produce pegozafermin for commercial supply. We cannot guarantee that BiBo will be able to complete or make operational the production facility in a timely manner or at all, or be able to scale up and produce the quantities we would require to commercialize pegozafermin. Under our Collaboration Agreement with BiBo, we are required to pay BiBo an aggregate of $135.0 million (exclusive of applicable value-added tax) toward the construction of the production facility, however, if the actual costs of the production facility are substantially greater than the estimated budget, we and Bibo will negotiate a means of allocating such cost overruns. We may be ultimately responsible for a substantial portion of such overruns and it could negatively impact our financial condition and results of operations. For additional information regarding the production facility, please see Part I, Item 7 “Management’s Discussion and Analysis of Financial Condition and Results of Operations—Contractual Obligations and Commitments” and Note 5 to our consolidated financial statements appearing under Part II, Item 8 of this Annual Report.

The terms of our commercial supply of pegozafermin may not be favorable to us and could have a material impact on our results of operations. There is no guarantee that our third-party manufacturers will be able to fulfill our supply needs. 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 any of our third-party manufacturers or vendors, including our fill-finish vendor, are not able to fulfill their supply or manufacturing obligations in a timely manner, our clinical trials may be delayed. In addition, 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.

We have begun producing certain of the reagents required for the glycoPEGylation at BTPH and Merck & Cie using the know-how transferred to us from Teva under our Reagent Supply and Technology Transfer Agreement. We have not completed the manufacturing process for all these reagents and cannot guarantee that we will be able to produce them successfully, or scale up our production for the quantities needed for commercialization.

Any significant delay in the acquisition or decrease in the availability of these raw materials from suppliers could considerably delay the manufacture of pegozafermin, which could adversely impact the timing of any planned trials or the regulatory approvals of pegozafermin.

We rely on third-party vendors for our assay development and testing. If such third-party vendors are unable to successfully produce or test such assays, it may substantially increase our cost or could adversely impact the timing of any planned trials or the regulatory approvals of pegozafermin.

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 cGMP. We 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 pegozafermin or any future product candidates and market our products following approval. Our primary source suppliers, BTPH and BiBo, have not yet manufactured a commercial product, and as a result, have not been subject to inspection by the FDA and other comparable foreign regulatory authorities.

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. Supply chain issues, including those resulting from the ongoing war in Ukraine and the acts of piracy and military unrest in the Red Sea, may affect our third-party vendors and cause delays. Furthermore, since we have engaged a manufacturer located in China, we are exposed to the possibility of product supply disruption and increased costs in the event of changes in the legislation or policies of the United States or Chinese governments, political unrest or unstable economic conditions in China. For example, WuXi Biologics, which we have engaged as a potential commercial supply chain vendor, is identified in the U.S. legislation known as the BIOSECURE Act, which was proposed in the 118th Congress, as a "biotechnology company of concern." The version of the BIOSECURE Act introduced in the U.S. House of Representatives during the 118th Congress would prohibit federal agencies from entering into procurement contracts with, as well as providing grants and loans to, an entity that uses biotechnology equipment or services from a biotechnology company of concern, and includes a grandfathering provision allowing biotechnology equipment and services provided or produced by named "biotechnology companies of concern" under a contract or agreement entered into before the effective date until January 1, 2032. The pathway and timing for the BIOSECURE Act or its provisions to become law are uncertain. Foreign CMOs may be subject to U.S. legislation, including the proposed BIOSECURE Act, trade restrictions, and other foreign regulatory requirements that could increase the cost or reduce the supply of material available to us, delay the procurement or supply of such material or have an adverse effect on our ability to secure significant commitments from governments to purchase our potential therapies. These and other risks associated with our collaboration with BiBo, based in China, may materially adversely affect our ability to attain or maintain quantities of pegozafermin needed for commercialization, if approved. In addition, we have agreed to arbitrate claims related to the Collaboration Agreement with BiBo in Shanghai under the laws of the People's Republic of China, which may limit our ability to enforce our contractual rights against BiBo. Changes to Chinese regulations or government policies affecting biopharmaceutical companies are unpredictable and may have a material adverse effect on our collaborators in China, which could have an adverse effect on our business, financial condition, results of operations and prospects. Developments in China's public health, economic, political, and social conditions and the uncertainty around China's relationship with other governments, such as the United States and the United Kingdom, could also negatively impact our ability to manufacture our product candidates for our planned clinical trials or have an adverse effect on our ability to secure government funding, which could adversely affect our financial condition and cause delay to our clinical development programs. Furthermore, if the BIOSECURE Act is passed and one or more of our collaborators in China is deemed to be a biotechnology company of concern, our operations and financial condition may be negatively impacted as a result of any delays or increased costs arising from the trade restrictions and other foreign regulatory requirements affecting such collaborators. 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 pegozafermin from BTPH or BiBo, which are our primary manufacturing sources for pegozafermin, 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.

Pegozafermin 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.

While we believe that pegozafermin has been generally well tolerated with a favorable safety profile in our clinical trials, patients have experienced adverse events that have been considered treatment-related. Some of the more common adverse events included diarrhea, nausea, injection site erythema, injection site rash and increase appetite. Undesirable side effects caused by pegozafermin or any future product candidates or by other companies' similar approved drugs or 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 pegozafermin or any future product candidates. As with other drugs, we have seen evidence of adverse effects in animal and human studies and it is possible that other adverse effects will become apparent in ongoing or future animal or human studies. 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 pegozafermin 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 pegozafermin or any future product candidates or approved products. Our Phase 1 and Phase 2 clinical trials have involved a limited number of patients and limited duration of exposure to pegozafermin. As a result, we cannot be assured that adverse effects of pegozafermin will not be uncovered when a larger number of patients are exposed to the product candidate in our Phase 3 clinical trials. Further, we expect that pegozafermin will require multiple administrations via subcutaneous injection in the course of a clinical trial. This chronic administration increases the risk that rare adverse events or chance findings are discovered in the commercial setting, where pegozafermin would be administered to more patients or for greater periods of time, that were not uncovered by our clinical drug development programs.

We are developing pegozafermin for the treatment of MASH and SHTG. The requirements for approval of pegozafermin by the FDA and comparable foreign regulatory authorities may be difficult to predict and may change over time, which makes it difficult to predict the timing and costs of the clinical development.

We are developing pegozafermin for the treatment of MASH. Although there are guidelines issued by the FDA and comparable foreign regulatory authorities for the development of drugs for the treatment of MASH, the development of a novel product candidates such as pegozafermin may 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 MASH therapies, we expect that the path for regulatory approval for MASH 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. In particular, regulatory authority expectations about liver biopsy data may evolve especially as more information is published about the inherent variability in liver biopsy data. Certain of our competitors have experienced regulatory setbacks for MASH therapies following communications from the FDA and comparable foreign regulatory authorities. We currently do not know the impact, if any, that these setbacks could have on the path for regulatory approval for MASH therapies generally or for pegozafermin. In addition, another company has received regulatory approval for its MASH therapy, and such approval could impact our development of pegozafermin. We may have difficulty enrolling patients in our Phase 3 program for patients with MASH if patients choose to take such approved drug, rather than enroll in a clinical trial. In addition, such approved MASH therapy will establish initial pricing and labelling expectations, which could impact our pricing and labelling if pegozafermin receives marketing approval.

We are also developing pegozafermin for the treatment of SHTG. Clinical trials for the treatment of SHTG may be relatively costly and time-consuming. In addition, the requirements for approval by the FDA and comparable foreign regulatory authorities may change over time. If the FDA or comparable foreign regulatory authorities require additional evidence in addition to our ongoing Phase 3 program in SHTG to support a successful submission for approval, we may be required to make changes to our program design that could impact timelines and cost.

Our anticipated development costs would likely increase if development of pegozafermin or any future product candidate is delayed because we are required by the FDA and comparable foreign regulatory authorities to perform studies or trials in addition to, or different from, those that we currently anticipate, or make changes to ongoing or future clinical trial designs. In addition, if we are unable to leverage our safety database for both SHTG and MASH indications, we may be required to perform additional trials, which would result in increased costs and may affect the timing or outcome of our clinical trials.

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, Novo Nordisk, Akero Therapeutics, Inc. and Boston Pharmaceuticals are also developing FGF21 product candidates for the treatment of MASH. 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 clinical development plans for pegozafermin or even the viability or prospects of pegozafermin 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.

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, pegozafermin has been manufactured by third-party manufacturers for preclinical studies and clinical trials. The process of manufacturing pegozafermin, and in particular, the glycoPEGylation process, is complex, highly regulated and subject to several risks and requires significant expertise and capital investment, including for the development of advanced manufacturing techniques and process controls. Manufacturers of biologic products often encounter difficulties in production, including 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 pegozafermin 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.

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

The biopharmaceutical industry is intensely competitive and subject to rapid innovation and significant technological advancements. 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. Certain of these companies have published positive data regarding their clinical trials, which may further increase the competition we face. 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 MASH 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 MASH and SHTG, will increase. We may also face competition indirectly from companies developing therapies like the incretins to treat obesity and/or Type 2 diabetes. Some incretin-based therapies are also being developed for the treatment of MASH.

There are numerous currently approved therapies for treating diseases other than MASH and some of these currently approved therapies may exert effects that could be similar to pegozafermin in MASH. 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. This

may make it difficult for us to differentiate our products from currently approved therapies, which may adversely impact our business strategy. We expect that if pegozafermin or any future product candidates are approved, they will be priced at a significant premium over competitive generic products, including branded generic products. Insurers and other third-party payors may also encourage the use of generic products or specific branded products prior to utilization of pegozafermin. In addition, many companies are developing new therapeutics, and we cannot predict what the standard of care will be as pegozafermin or any future product candidates progress through clinical development. In addition, to the extent pegozafermin or any future product candidates are approved for liver or 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 pegozafermin 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.

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. 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. 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.

Unstable market and economic conditions, inflation, fluctuations in interest rates, natural disasters, public health crises, political crises, geopolitical events, such as the crisis in Ukraine and Israel, or other macroeconomic conditions, may have serious adverse consequences on our business and financial condition.

The global economy, including credit and financial markets, have experienced extreme volatility and disruptions at various points over the last few decades, including, among other things, diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, supply chain shortages, increases in inflation rates, fluctuating interest rates, and uncertainty about economic stability. In addition, the effects of global economic conditions, including new or increased tariffs and other barriers to trade, trade and other international disputes, slower growth or recession, high unemployment, labor availability constraints, significant natural disasters, including as a result of climate change, changes to fiscal and monetary policy or government budget dynamics, particularly in the pharmaceutical and biotech areas, may have adverse effects on our business and financial condition. For example, public health crises have resulted in widespread unemployment, economic slowdown and extreme volatility in the capital markets. In addition, the Federal Reserve has previously raised interest rates multiple times in response to concerns about inflation and it may raise them again. Fluctuation in interest rates, coupled with reduced government spending and volatility in financial markets, may increase economic uncertainty and affect consumer spending. Similarly, the ongoing military conflicts between Russia and Ukraine and between Israel and surrounding areas and the rising tensions between China and Taiwan have created extreme volatility in the global capital markets and may have further global economic consequences, including disruptions of the global supply chain. Any such volatility and disruptions may adversely affect our business or the third parties on whom we rely. If the equity and credit markets deteriorate, including as a result of political unrest or war, 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 have experienced and may in the future experience disruptions as a result of such macroeconomic conditions, including delays or difficulties in initiating or expanding clinical trials and manufacturing sufficient quantities of

materials. Any one or a combination of these events could have a material and adverse effect on our results of operations and financial condition.

The Loan Agreement contains certain covenants that could adversely affect our operations and, if an event of default were to occur, we could be forced to repay any outstanding indebtedness sooner than planned and possibly at a time when we do not have sufficient capital to meet this obligation.

Pursuant to the Loan Agreement, we have pledged substantially all of our assets, other than our intellectual property rights, and have agreed that we may not sell or assign rights to our patents and other intellectual property without the prior consent of our lenders. Additionally, the Loan Agreement contains certain affirmative and negative covenants that could prevent us from taking certain actions without the consent of our lenders. These covenants may limit our flexibility in operating our business and our ability to take actions that might be advantageous to us and our stockholders. The Loan Agreement also includes customary events of default, including, among other things, an event of default upon a change of control. Upon the occurrence and continuation of an event of default, all amounts due under the Loan Agreement become automatically (in the case of a bankruptcy event of default) or may become (in the case of all other events of default and at the option of the administrative agent), immediately due and payable. If an event of default under the Loan Agreement should occur and be continuing, we could be required to immediately repay any outstanding indebtedness. If we are unable to repay such debt, the lenders would be able to foreclose on the secured collateral, including our cash accounts, and take other remedies permitted under the Loan Agreement. Even if we are able to repay such accelerated debt amount under the Loan Agreement upon an event of default, the repayment of these sums may significantly reduce our working capital and impair our ability to operate as planned.

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

We are in the early stages of building the full team that we anticipate we will need to complete the development pegozafermin and other future product candidates. 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 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. 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 experience difficulty in adjusting to our growth and strategic focus.

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 in the biotechnology and pharmaceutical industries. If we are not able to attract and retain necessary personnel and consultants to accomplish our business objectives, it may significantly impede the achievement of our development and commercial objectives and our ability to implement our business strategy. In addition, we are highly dependent on the development, regulatory, manufacturing, commercialization and financial 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.

We rely on third parties for certain aspects of our product candidate development process and 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. If these third parties do not successfully perform and comply with regulatory requirements, we may not be able to successfully complete clinical development, obtain regulatory approval, or commercialize our product candidates and our business could be substantially harmed.

We depend on collaborators, partners, licensees, clinical investigators, contract research organizations, 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 and to manufacture clinical and commercial scale quantities of our drug substance and drug product and expect to depend on these third parties to market, sell and distribute any products we successfully develop. 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. 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 pegozafermin or any future product candidates, producing additional losses and depriving us of potential revenue.

In addition, we have relied upon and plan to continue to rely upon third party contract research organizations ("CROs") to conduct, monitor, and manage preclinical and clinical programs. We rely on these parties for execution of clinical trials, and we manage and control only some aspects of their activities. We remain responsible for ensuring that each of our trials is conducted in accordance with the applicable protocol, legal, regulatory, and scientific standards, and our reliance on the CROs does not relieve us of our regulatory responsibilities. We and our CROs and other vendors are required to comply with all applicable laws, regulations, and guidelines, including those required by the FDA, EMA and comparable foreign regulatory authorities for all of our product candidates in clinical development. If we or any of our CROs or vendors fail to comply with applicable and evolving laws, regulations, and guidelines, the results generated in our clinical trials may be deemed insufficient or unreliable, and the FDA, EMA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications.

Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses.

Our operations, and those of our contract research organizations, CMO, suppliers, and other contractors and consultants, could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, acts of war, medical pandemics or epidemics, such as the novel coronavirus, and other natural or man-made disasters or business interruptions. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses.

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

Although the development and commercialization of pegozafermin 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 MASH 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.

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.

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. Collaborations are complex and time-consuming to negotiate and document. 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.

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

We 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.

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 subjects us to U.S. and foreign governmental trade, import and export, and customs regulations and laws including various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Controls and the U.S. Export Administration Regulations. Compliance with these regulations and laws is costly and exposes us to penalties for non-compliance. Doing business internationally potentially involves a number of risks, any of which could harm our ongoing international clinical operations and supply chain, as well as any future international expansion and operations and, consequently, our business, financial condition, prospects and results of operations.

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

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we 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. Our clinical trial liability insurance coverage may not adequately cover all liabilities that we may incur.

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. 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 laws.

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 information technology, 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. From time to time, we are subject to periodic phishing attempts. In 2021, we implemented remedial measures promptly following a business email compromise caused by phishing, however, we cannot guarantee that our implemented remedial measures will prevent additional related, as well as unrelated, incidents. If a material system failure, accident or security breach 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.

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. 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.

If the market opportunities for our approved product candidates, if any, are smaller than we expect, it could materially and adversely affect our financial condition and results of operation.

If the market opportunity for our products, if approved, is smaller than we expect, we may never become or remain profitable nor generate sufficient revenue growth to sustain our business even if we obtain significant market share for them. The potentially addressable patient population for our products may be limited or may not be amenable to treatment with our products, and new patients may become increasingly difficult to identify or access, which would adversely affect our results of operations and our business.

Risks Related to Regulatory Approvals

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

We do not expect pegozafermin or any future product candidate to be commercially available for several years, if at all. Pegozafermin 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 pegozafermin 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.

While the FDA has approved a product for the treatment of MASH and there are guidelines issued by the FDA for the development of drugs for the treatment of MASH, it is unclear whether the requirements for approval will change in the future or whether the FDA will rely on regulatory precedent for future regulatory approvals. Any such changes may require us to conduct new trials that could delay our timeframe and increase the costs of our programs related to pegozafermin or any future product candidate for the treatment of MASH or SHTG.

Even if we are able to obtain regulatory approvals for pegozafermin 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 pegozafermin 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. Based on guidelines issued by the FDA for the development of drugs for the treatment of MASH, if pegozafermin 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 MASH. Under the Food and Drug Omnibus Reform Act of 2022, the FDA may require, as appropriate, that such studies be underway prior to approval or within a specific time period after the date of approval for a product granted accelerated approval. If pegozafermin 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 pegozafermin 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 pegozafermin 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 pegozafermin or any future product candidates will ever obtain regulatory approval. Pegozafermin or any future product candidate could fail to receive regulatory approval from the FDA or comparable foreign regulatory authorities for many reasons, including those referenced in Part I, Item 1. "Business— Government Regulation and Product Approval" in this Annual Report on Form 10-K. 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 the product candidate.

We have received Breakthrough Therapy designation for pegozafermin in MASH from the FDA and PRIME designation for pegozafermin in MASH from the EMA, but such designation may not actually lead to a faster development or regulatory review or approval process, and does not increase the likelihood that pegozafermin will receive marketing approval. In addition, we may seek Breakthrough Therapy, Fast Track or PRIME designation for other indications or future product candidates, but we might not receive such designation.

In September 2023, we received Breakthrough Therapy designation for pegozafermin in MASH from the FDA and in March 2024, the EMA granted PRIME status to pegozafermin in patients with MASH. We may in the future seek Breakthrough Therapy designation, Fast Track designation or PRIME designation for other indications or future product candidates. However, even if we believe a particular product candidate is eligible for these designations, we cannot assure you that the FDA, EMA or similar regulatory agency would decide to grant them.

In addition, breakthrough Therapy, Fast Track and PRIME designations may not result in a faster development process, review or approval compared to conventional FDA or EMA procedures, respectively. In addition, even though pegozafermin is designated as a Breakthrough Therapy in MASH, the FDA may later decide that the product candidate no longer meets the conditions for designation and the designation may be rescinded. The Breakthrough Therapy, Fast Track and PRIME designations do not assure ultimate regulatory approval by the FDA or the EMA. Many drugs and biologics that have received Breakthrough Therapy, Fast Track or PRIME designation have failed to obtain approval. See Part I, Item 1. "Business—Expedited Programs for Serious Conditions" in this Annual Report on Form 10-K.

We conduct clinical trials for pegozafermin at sites outside the United States, and the FDA may not accept data from trials conducted in such locations.

We have conducted and expect to continue conducting one or more of our clinical trials outside the United States. Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of this data is subject to conditions imposed by the FDA. For example, the clinical trial must be well designed and conducted and performed by qualified investigators in accordance with ethical principles. The trial population must also adequately represent the U.S. population, and the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful. In addition, while these clinical trials are subject to the applicable local laws, FDA acceptance of the data will depend on its determination that the trials also complied with all applicable U.S. laws and regulations. If the FDA does not accept the data from any trial that we conduct outside the United States, it would likely result in the need for additional trials, which would be costly and time-consuming and would delay or permanently halt our development of the applicable product candidates. Even if the FDA accepted such data, it could require us to modify our planned clinical trials to receive clearance to initiate such trials in the United States or to continue such trials once initiated.

Further, conducting international clinical trials presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled patients in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs that could restrict or limit our ability to conduct our clinical trials, the administrative burdens of conducting clinical trials under multiple sets of foreign regulations, foreign exchange fluctuations, diminished protection of intellectual property in some countries, as well as political and economic risks relevant to foreign countries.

Disruptions at the FDA and other government agencies could negatively affect the review of our regulatory submissions, which could negatively impact our business.

The ability of the FDA to review and approve regulatory submissions can be affected by a variety of factors, including disruptions caused by government shutdowns and public health crises, or layoffs of federal workers by the federal government. Such disruptions could significantly impact the ability of the FDA or other regulatory authorities to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Even if pegozafermin 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. 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.

We expect the product candidates we develop will be regulated as biologics, and therefore they may be subject to competition sooner than anticipated.

The BPCIA was enacted as part of the ACA to establish an abbreviated pathway for the approval of biosimilar and interchangeable biological products. The regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as "interchangeable" based on its similarity to an approved biologic. Under the BPCIA, an application for a biosimilar product cannot be approved by the FDA until 12 years after the reference product was approved under a BLA. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when processes intended to implement BPCIA may be fully adopted by the FDA, any of these processes could have a material adverse effect on the future commercial prospects for our biological products.

We believe that any of the product candidates we develop that is approved in the United States as a biological product under a BLA should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider the subject product candidates to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of the reference products in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

In addition, the first biologic product submitted under the abbreviated approval pathway that is determined to be interchangeable with the reference product has exclusivity against other biologics submitted under the abbreviated approval pathway for the lesser of (i) one year after the first commercial marketing, (ii) 18 months after approval if there is no legal challenge, (iii) 18 months after the resolution in the applicant's favor of a lawsuit challenging the biologics' patents if an application has been submitted, or (iv) 42 months after the application has been approved if a lawsuit is ongoing within the 42-month period. The approval of a biologic product biosimilar to one of our product candidates could have a material adverse impact on our business as it may be significantly less costly to bring to market and may be priced significantly lower than our product candidates.

Current and future legislation may increase the difficulty and cost for us, and any collaborators, to obtain marketing approval of and commercialize our drug candidates and affect the prices we, or they, may obtain.

Heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products has resulted in several recent Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for

products. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare therapies, which could result in reduced demand for our product candidates or additional pricing pressures. The Inflation Reduction Act of 2022 ("IRA") includes several measures intended to lower the cost of prescription drugs and related healthcare reforms. We cannot be sure whether additional legislation or rulemaking related to the IRA will be issued or enacted, or what impact, if any, such changes will have on the profitability of any of our drug candidates, if approved for commercial use, in the future.

Healthcare insurance coverage and reimbursement may be limited or unavailable for our product candidate, if approved, which could make it difficult for us to sell our product candidate or other therapies profitably.

The success of pegozafermin, if approved, depends on the availability of coverage and adequate reimbursement from third-party payors including governmental healthcare programs, such as Medicare and Medicaid, commercial payors, and health maintenance organizations. We cannot be sure that coverage and reimbursement will be available for, or accurately estimate the potential revenue from, our product candidates or assure that coverage and reimbursement will be available for any product that we may develop.

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenue, if any.

In some countries, particularly the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations. To obtain coverage and reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our drug candidate to other available procedures. If reimbursement of our drugs is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

Risks Related 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. 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 pegozafermin 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 pegozafermin or any future product candidates.

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. Historically, 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. Accordingly, even if we or our licensors are able to obtain patents, the patents might be substantially narrower than anticipated. Thus, there is no assurance as to the degree and range of protections any of our patents, if issued, may afford us or whether patents will be issued. 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. 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.

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. 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 pegozafermin or any future product candidates and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

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 pegozafermin. 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 the FGF21 Agreement with Teva under which we acquired certain patents, intellectual property and other assets relating to Teva's glycoPEGylated FGF21 program, including pegozafermin. Under this agreement, we were granted a perpetual, non-exclusive (but exclusive as to pegozafermin), non-transferable, worldwide license to patents and know-how related to glycoPEGylation technology used in the development, manufacture and commercialization of pegozafermin and products containing pegozafermin. The FGF21 Agreement also contains numerous covenants with which we must comply, including the utilization of commercially reasonable efforts to develop and ultimately commercialize pegozafermin, as well as certain reporting covenants and the obligation to make royalty payments, if and when pegozafermin 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 pegozafermin and products containing pegozafermin. 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.

We may be unable to obtain intellectual property rights or technology necessary to develop and commercialize pegozafermin 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 pegozafermin. 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 pegozafermin 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.

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. 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.

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 pegozafermin or any future product candidates or force us to cease some of our business operations, which could materially harm our business.

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 product candidates. Thus, we cannot guarantee that our product candidates, or our commercialization thereof, do not and will not infringe any third party's intellectual property.

Risks Related to Ownership of Our Common Stock

The price of our common stock may be volatile and fluctuate significantly and results announced by us and our collaborators or competitors could cause our stock price to decline, 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. Our stock price could fluctuate significantly due to various factors in addition to those otherwise described in this Annual Report on Form 10-K, including those described in these "Risk Factors," including business developments announced by us and by our collaborators and competitors, or as a result of market trends and daily trading volume. The business developments that could affect our stock price include announcements or disclosures from competitors in the same class or category, new collaborations, clinical advancement, commercial launch or discontinuation of product candidates in the same class or category and regulatory approvals for our product candidates or product candidates in the same class or category. Our stock price could also fluctuate significantly with the level of overall investment interest in small-cap biotechnology stocks or for other reasons unrelated to our business. 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.

Sales of our common stock, or the perception that such sales may occur, or issuance of shares of our common stock upon exercise of warrants 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. 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 Plan and the Amended and Restated 2023 Inducement 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. Further, as opportunities present themselves, we may enter into financing or similar arrangements in the future, including the issuance of debt or equity securities.

In addition, if we issue warrants in the future, we may need to settle exercises of such warrants in shares of our common stock. The issuance of shares of our common stock upon exercise of warrants will dilute the ownership interests of our stockholders, which could depress the trading price of our common stock. In addition, the market's expectation that exercises may occur could depress the trading price of our common stock even in the absence of actual exercises. Moreover, the expectation of exercises could encourage the short selling of our common stock, which could place further downward pressure on the trading price of our common stock.

Certain of our executive officers and directors have entered or may enter into Rule 10b5-1 plans providing for sales of shares of our common stock from time to time. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the executive officer or director when entering into the plan, without further direction from the executive officer or director. A Rule 10b5-1 plan may be amended or terminated in some circumstances. Our executive officers and directors also may buy or sell additional shares outside of a Rule 10b5-1 plan when they are not in possession of material nonpublic information.

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, including under the 2023 ATM Facility (defined below), 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.

We may issue warrants in the future, and hedging activity by investors in such warrants could depress the trading price of our common stock.

We may issue warrants in the future and investors in such warrants may seek to employ an arbitrage strategy. Under this strategy, investors typically short sell a certain number of shares of our common stock and adjust their short position over time while they continue to hold the warrants. Investors may also implement this type of strategy by entering into swaps on our common stock in lieu of, or in addition to, short selling shares of our common stock. This market activity, or the market's perception that it will occur, could depress the trading price of our common stock.

General Risk Factors

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 December 31, 2024, 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.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud. If we are unable to maintain effective internal control over financial reporting, investors may lose confidence in the accuracy and completeness of our financial reports and the market price of our stock may decrease.

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

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

The Sarbanes-Oxley Act of 2002 (the "Sarbanes-Oxley Act") requires, among other things, that we maintain effective internal controls for financial reporting and disclosure controls and procedures. In particular, we are required to perform system and process evaluation and testing of our internal controls over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting, as required by Section 404(a) of the Sarbanes-Oxley Act. Section 404(b) of the Sarbanes-Oxley Act ("Section 404") also requires our independent auditors to express an opinion on our internal control over financial reporting. Ensuring that we have adequate internal controls in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that will need to be evaluated frequently. If we are unable to maintain effective internal control over financial reporting, we may not have adequate, accurate or timely financial information, our independent registered public accounting firm may issue a report that is adverse, and we may be unable to meet our reporting obligations as a public company or comply with the requirements of the SEC or Section 404. This could result in a restatement of our financial statements, the imposition of sanctions, including the inability of registered broker dealers to make a market in our common stock, or investigation by regulatory authorities. Any such action or other negative results caused by our inability to meet our reporting requirements or comply with legal and regulatory requirements or by disclosure of an accounting, reporting or control issue could adversely affect the trading price of our securities and our business. Material weaknesses in our internal control over financial reporting could also

reduce our ability to obtain financing or could increase the cost of any financing we obtain. If we are not able to comply with the requirements of Section 404 or if we or our independent registered public accounting firm are unable to express an opinion as to the effectiveness of our internal control over financial reporting, investors may lose confidence in the accuracy and completeness of our financial reports, the market price of our stock could decline and we could be subject to sanctions or investigations by Nasdaq, the SEC, or other regulatory authorities, which would require additional financial and management resources.

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. In addition, 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 certain actions or proceedings under Delaware statutory or common law. 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. 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, we may incur additional costs associated with resolving such action in other jurisdictions.

Our ability to use our net operating loss carryforwards and other tax attributes may be limited. If we are required to pay any tax assessment, it could impact our net operating loss carryforwards, as well as our results of operations and financial condition.

As of December 31, 2024, we had U.S. federal and state net operating loss ("NOL") carryforwards of $255.5 million and $496.5 million, respectively, which may be available to offset future taxable income. As of December 31, 2024, we also had gross federal tax credits of $19.7 million, which may be used to offset future tax liabilities. Certain NOLs and tax credit carryforwards will begin to expire in 2039. Use of our NOL carryforwards and tax credit carryforwards depends on many factors, including having current or future taxable income, which cannot be assured.

In addition, in December 2023, the Israeli Tax Authorities issued a tax assessment claiming our 2019 reorganization and intercompany transaction to license the intellectual property rights from our subsidiary in Israel should be treated as a sale of intellectual property rights. As of December 31, 2024, discussions with the Israel Tax Authorities are ongoing. If this matter is litigated and the Israeli Tax Authorities are able to successfully sustain their position and we are required to pay a tax assessment, it could impact our NOL carryforwards and our results of operations and financial condition could be materially and adversely affected. See further discussion in Part II, Item 7 "Management's Discussion and Analysis of Financial Condition and Results of Operations—Critical Accounting Estimates—Income Taxes" and in Note 9 to our consolidated financial statements appearing under Part II, Item 8 of this Annual Report on Form 10-K.

Litigation costs and the outcome of litigation could have a material adverse effect on our business.

From time to time we may be subject to litigation claims through the ordinary course of our business operations regarding, but not limited to, securities litigation, employment matters, security of patient and employee personal information, contractual relations with collaborators and licensors and intellectual property rights. Litigation to defend ourselves against claims by third parties, or to enforce any rights that we may have against third parties, could result in substantial costs and diversion of our resources, causing a material adverse effect on our business, financial condition, results of operations or cash flows.

Item 1B. Unresolved Staff Comments.

None.

Item 1C. Cybersecurity.

Risk Management and Strategy

We have implemented procedures for assessing, identifying and managing significant risks from cybersecurity threats and have incorporated these procedures into our overall risk management systems and processes. We regularly evaluate significant risks from cybersecurity attacks, including any potential unauthorized occurrence on or conducted through our information systems that may result in adverse effects on the confidentiality, integrity, or availability of our information systems or any information stored there. The program to manage cybersecurity risks has tools and activities designed to identify, examine and manage current and potential cybersecurity threats, as well as plans and strategies designed to deal with threats and incidents.

We regularly evaluate the cybersecurity risks that could affect our information systems, as well as on an ad hoc basis when there is a significant change in how we do business that may increase the exposure of our information systems to such risks. These evaluations include identifying the possible internal and external risks, how likely and harmful they are, and whether our current policies, procedures, systems, and safeguards are adequate to handle them.

We use these risk assessments to design, implement, and maintain appropriate safeguards that are intended to mitigate identified risks, address any shortcomings in our existing safeguards, and regularly check how well our safeguards work. Our information technology ("IT") department is primarily responsible for evaluating, overseeing, and handling our cybersecurity risks to manage the process of risk assessment and mitigation. We have established a cross-functional IT Security Steering Committee that oversees the management of our cybersecurity risks and execution of any mitigation efforts.

Our IT department and Company management work together to check and improve our safeguards as part of our overall risk management system. We also periodically provide training to our employees on these safeguards and keep them informed of our cybersecurity policies through regular communications across the Company.

We work with consultants or other third parties as part of our risk assessment processes, when appropriate. They help us create and execute our cybersecurity policies and procedures and check and test our safeguards. We ask key third-party service providers to confirm that it can apply and keep appropriate cybersecurity measures in line with all relevant laws, to apply and keep reasonable cybersecurity measures when they work with us, and to promptly report any possible breach of their cybersecurity measures that could impact our company.

Since the beginning of the last fiscal year, we have not identified risks from known cybersecurity threats, including as a result of any previous cybersecurity incidents, that have materially affected us, including our business strategy, results of operations or financial condition, but we face certain ongoing cybersecurity risks threats that, if realized, are reasonably likely to materially affect us. For additional information regarding these risks, please refer to Item 1A, "Risk Factors," "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 this Annual Report on Form 10-K.

Governance

Our board of directors oversees our overall risk management process and significant risks facing us, including cybersecurity risks. The audit committee, which is comprised solely of independent directors, has been designated by our board of directors to oversee cybersecurity risks. Our board of directors oversees and evaluates strategic risk exposure, while our executive officers manage the significant risks we encounter on a daily basis.

The audit committee receives periodic briefings from our Chief Financial Officer, the Chair of the IT Security Steering Committee, regarding our cybersecurity risks and activities, including any recent cybersecurity incidents

and related responses, cybersecurity systems testing, and activities of third parties. Our audit committee provides periodic updates to the board of directors on such reports.

The IT Security Steering Committee, which is in charge of our cybersecurity policies and procedures, including the ones discussed in "Risk Management and Strategy" above, is led by our Chief Financial Officer, who has nine years of senior leadership experience at public biotechnology companies, including six years with 89bio. The IT Security Steering committee also includes our Director of IT, who is an experienced Information Technology professional and has over 20 years of experience managing information technology, of which more than 10 years pertain to cybersecurity related experience.

Item 2. Properties.

Our corporate headquarters is located in San Francisco, California, and consists of 17,616 square feet of office space under a lease that expires in March 2027. We believe that our current space is 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 has been listed on The Nasdaq Global Market under the symbol "ETNB" since November 11, 2019. Prior to that date, there was no public trading market for our common stock.

Holders of Record

As of February 24, 2025, there were approximately five stockholders of record of our common stock. Since many of our shares of common stock are held by brokers and other institutions on behalf of stockholders, we are unable to estimate the total number of stockholders represented by these record holders.

Dividend Policy

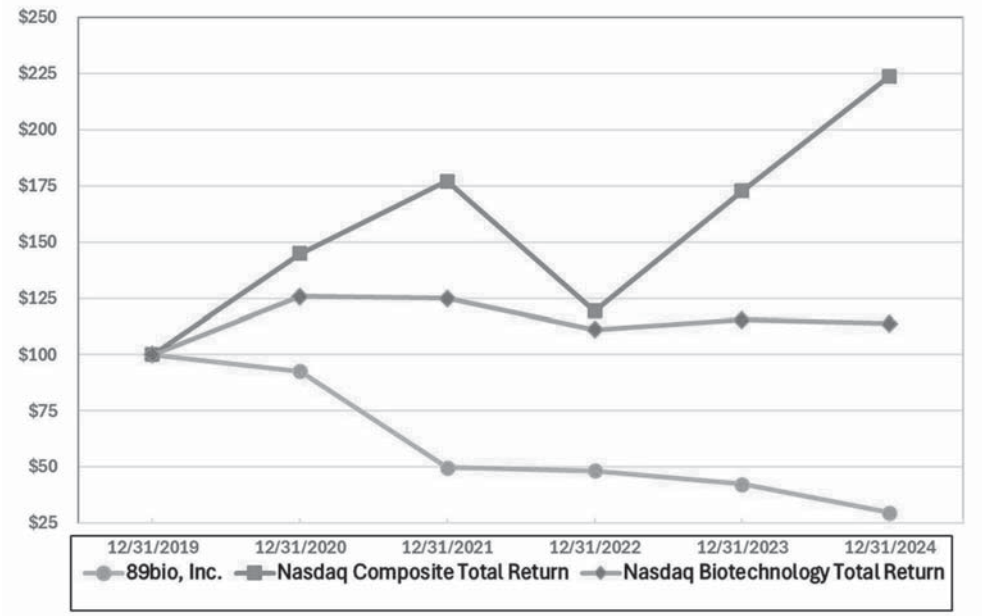
We have never declared or paid cash dividends on our capital stock and have no present intention to pay cash dividends on our common stock for the foreseeable future. Any determination to pay dividends to holders of our common stock will be at the discretion of our board of directors and will depend 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.

Stock Performance Graph

The following is not deemed "filed" with the Securities and Exchange Commission and is not to be incorporated by reference into any filing we make under the Securities Act of 1933, as amended, whether made before or after the date hereof and irrespective of any general incorporation by reference language in such filing.

The graph below compares the five-year cumulative total stockholder return of $100 (and the reinvestment of any dividends thereafter) on December 31, 2019 (the last trading day for the year ended December 31, 2019) in (i) our common stock, (ii) the Nasdaq Composite Index and (iii) the Nasdaq Biotechnology Index. The stock price performance reflected in the graph below is not necessarily indicative of future performance.

Comparison of 5-Year Cumulative Total Return*
Among 89bio Inc., the Nasdaq Composite Index and the Nasdaq Biotechnology Index



***$100 INVESTED ON DECEMBER 31, 2019 IN STOCK OR INDEX (INCLUDING REINVESTMENT OF DIVIDENDS)**

	12/31/2019	12/31/2020	12/31/2021	12/31/2022	12/31/2023	12/31/2024
89bio, Inc.	$ 100.00	$ 92.70	$ 49.71	$ 48.42	$ 42.49	$ 29.75
Nasdaq Composite Total Return	$ 100.00	$ 144.92	$ 177.06	$ 119.45	$ 172.77	$ 223.87
Nasdaq Biotechnology Total Return	$ 100.00	$ 126.42	$ 126.45	$ 113.65	$ 118.87	$ 118.20

Recent Sales of Unregistered Securities

None.

Issuer Purchases of Equity Securities

None.

Item 6. Reserved

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, pegozafermin, a specifically engineered glycoPEGylated analog of fibroblast growth factor 21 ("FGF21"), is currently being developed for the treatment of metabolic dysfunction-associated steatohepatitis ("MASH"), previously known as nonalcoholic steatohepatitis, and for the treatment of severe hypertriglyceridemia ("SHTG"). Refer to the section titled "Business" in Part I, Item 1 of this Annual Report on Form 10-K for additional information related to our clinical development programs in MASH and SHTG.

We commenced operations in 2018 and have devoted substantially all of our resources to raising capital, acquiring our initial product candidate, identifying and developing pegozafermin, licensing certain related technology, conducting research and development activities (including preclinical studies and clinical trials) and providing general and administrative support for these activities.

In April 2024, we entered into a collaboration agreement (the "Collaboration Agreement") with BiBo Biopharma Engineering Co., Ltd. ("BiBo"), pursuant to which BiBo will construct a production facility specifically designed to supply us with pegozafermin for commercialization, if approved (the "Production Facility"). Pursuant to the Collaboration Agreement, BiBo will build the Production Facility at BiBo's facility in the Lin-gang Special Area of China (Shanghai) Pilot Free Trade Zone to manufacture the bulk active ingredient (the "Drug Substance") required to produce pegozafermin for commercial supply. The platform is expected to provide us with manufacturing capacity to meet our commercial needs.

We expect our existing cash, cash equivalents and marketable securities of $440.0 million as of December 31, 2024, supplemented by $269.9 million in net proceeds from our February 2025 equity offering, will be sufficient to fund our planned operating expenses and capital expenditure requirements for a period of at least one year following the filing of this Form 10-K.

We have incurred net losses since our inception. Our net losses for the years ended December 31, 2024, 2023 and 2022 were $367.1 million, $142.2 million and $102.0 million, respectively. As of December 31, 2024, we had an accumulated deficit of $824.5 million. We expect to continue to incur significant expenses and increasing operating losses as we advance pegozafermin and any future product candidates through clinical trials, seek regulatory approval for pegozafermin 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 pegozafermin 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.

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, pegozafermin. 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 incurred pursuant to the Collaboration Agreement with BiBo, 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 stock-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 services are provided based on invoices and statements received from our external service providers and by monitoring the status of their activities. We adjust our accrued expenses 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 payment becomes probable and reasonably estimable, which is generally upon achievement of the milestone.

We expect our research and development expenses to increase for the foreseeable future as we continue the development of pegozafermin 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 pegozafermin and any future product candidates is highly uncertain. To the extent that pegozafermin 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 pegozafermin 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 pegozafermin or any future product candidate.

General and Administrative Expenses

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, employee benefits and stock-based compensation for personnel in executive, finance, commercial 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.

Interest Expense

Interest expense consists of cash interest related to our term loan facility, noncash interest attributable to the accretion of end of term loan fees, amortization of deferred debt issuance costs related to our term loan facility and loss on extinguishment of debt.

Interest Income and Other, Net

Interest income and other, net is primarily comprised of interest income derived from marketable securities, including the accretion of discounts and amortization of premiums.

Income Taxes

We make estimates of the amounts to recognize for income taxes in each tax jurisdiction in which we operate. In addition, provisions are established for uncertain tax positions taken.

Results of Operations

A discussion regarding our financial condition and results of operations for the year ended December 31, 2024 compared to the year ended December 31, 2023 is presented below. A discussion regarding our financial condition and results of operations for the year ended December 31, 2023 compared to the year ended December 31, 2022 can be found in “Management’s Discussion and Analysis of Financial Condition and Results of Operations” in our Annual Report on Form 10-K filed with the SEC on March 1, 2024.

Comparison of the Years Ended December 31, 2024 and 2023

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

	Year Ended December 31,		
	2024	2023	Change
Operating expenses:			
Research and development	$ 345,037	$ 122,230	$ 222,807
General and administrative	39,619	28,974	10,645
Total operating expenses	384,656	151,204	233,452
Loss from operations	(384,656)	(151,204)	(233,452)
Interest expense	(5,290)	(4,794)	(496)
Interest income and other, net	23,559	17,676	5,883
Income tax expense	(692)	(3,867)	3,175
Net loss	$ (367,079)	$ (142,189)	$ (224,890)

Research and Development Expenses

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

	Year Ended December 31,		
	2024	2023	Change
Contract manufacturing	$ 209,223	$ 52,799	$ 156,424
Clinical development	100,048	44,684	55,364
Personnel-related expenses	32,400	23,028	9,372
Other expenses	3,366	1,719	1,647
Total research and development expenses	$ 345,037	$ 122,230	$ 222,807

Research and development expenses increased by $222.8 million to $345.0 million in 2024, compared to $122.2 million in 2023. This increase was primarily attributable to a $156.4 million increase in contract manufacturing costs, which included $121.5 million (net of applicable value-added tax) in milestone payments made to BiBo pursuant to the Collaboration Agreement to secure manufacturing capacity to produce pegozafermin for our commercial needs. The remaining increase in contract manufacturing costs was primarily related to the supply of pegozafermin and clinical materials for our three Phase 3 clinical trials. Clinical development costs also increased by $55.4 million primarily due to the initiation and continuation of our Phase 3 clinical trials. Additionally, personnel-related expenses, including stock-based compensation, increased by $9.4 million primarily due to increased headcount.

General and Administrative Expenses

General and administrative expenses increased by $10.6 million to $39.6 million in 2024, compared to $29.0 million in 2023. This increase was primarily attributable to a $5.4 million increase in personnel-related expenses, including a $2.3 million increase in stock-based compensation, reflecting higher headcount to support our growth. The increase was also driven by a $3.7 million increase in consulting and professional fees and a $1.5 million increase in facilities and other costs.

Interest Expense

Interest expense increased by $0.5 million to $5.3 million in 2024 from $4.8 million in 2023. This increase was primarily attributable to higher average debt balances and interest rates in 2024 compared to 2023.

Interest Income and Other, Net

Interest income and other, net increased by $5.9 million to $23.6 million in 2024 from $17.7 million in 2023. This increase was primarily attributable to increased average investment balances and higher average yields earned on those balances in 2024, compared to 2023.

Income Tax Expense

Income tax expense decreased by $3.2 million to $0.7 million in 2024 from $3.9 million in 2023. The 2023 income tax expense primarily related to a provision for uncertain tax positions. Refer to Note 9 to our consolidated financial statements appearing under Part II, Item 8 of this Annual Report for additional discussion.

Liquidity and Capital Resources

To date, we have incurred significant net losses and negative cash flows from operations. As of December 31, 2024, we had cash, cash equivalents and marketable securities of $440.0 million and an accumulated deficit of $824.5 million.

Sources of Liquidity

At-the-Market ("ATM") Offerings

In March 2021, we entered into an ATM sales agreement (as amended, the "Sales Agreement") with Leerink Partners LLC and Cantor Fitzgerald & Co. (the "Sales Agents") pursuant to which we may offer and sell up to $75.0 million of shares of our common stock (the "2021 ATM Facility") from time to time pursuant to an effective registration statement. The Sales Agents are entitled to compensation at a commission of up to 3.0% of the aggregate gross sales price per share sold under the Sales Agreement. In February 2023, we entered into an amendment to the Sales Agreement, establishing a new ATM facility with an aggregate offering amount of up to $150.0 million of shares of our common stock (the "2023 ATM Facility") pursuant to an effective registration statement.

In 2023, we sold 2,168,539 shares of our common stock under the 2021 ATM Facility and 2023 ATM Facility and received net proceeds of $37.1 million.

In 2024, we sold 1,396,888 shares of our common stock under the 2023 ATM Facility and received net proceeds of $21.0 million. There were no sales under the 2023 ATM facility for the three months ended December 31, 2024. As of December 31, 2024, there was $104.4 million remaining for future sales under the 2023 ATM Facility.

Underwritten Public Offerings

In March 2023, we completed an underwritten public offering of our common stock and raised net proceeds of $296.8 million, after deducting underwriting discounts and commissions of $19.0 million and other offering costs of $0.5 million. In December 2023, we completed an underwritten public offering of our common stock and pre-funded warrants to purchase shares of our common stock and raised net proceeds of $161.8 million, after deducting underwriting discounts and commissions of $10.4 million and other offering costs of $0.4 million.

In November 2024, we completed an underwritten public offering of our common stock and pre-funded warrants to purchase shares of our common stock and raised net proceeds of $136.3 million, after deducting underwriting discounts and commissions of $7.2 million and other offering costs of $0.3 million.

In February 2025, we completed an underwritten public offering of our common stock and pre-funded warrants to purchase shares of common stock and raised net proceeds of $269.9 million, after deducting underwriting discounts and commissions of $17.3 million and other offering costs of $0.3 million.

Exercises of Common Stock Warrants

In 2023, warrants to purchase 2,927,570 shares of our common stock were exercised for cash generating proceeds of $15.6 million.

In 2024, pre-funded warrants to purchase 799,906 shares of our common stock were exercised via cashless exercises and warrants to purchase 10,179,789 shares of our common stock were exercised for cash generating proceeds of $54.2 million resulting in the issuance of a total of 10,979,695 shares of common stock.

Term Loan Facility

In January 2023, we entered into a Loan and Security Agreement (the "Original Loan Agreement") with the lender parties thereto (the "Lenders"), K2 HealthVentures LLC as administrative agent and Ankura Trust Company, LLC as collateral agent. The Original Loan Agreement provided for a term loan facility with a maximum aggregate principal of $100.0 million, consisting of up to four separate delayed-draw term loans ("Initial Term Loan"). Upon execution of the agreement, we drew $25.0 million pursuant to the Original Loan Agreement. An additional $25.0 million expired undrawn and $50.0 million available at the Lenders' discretion lapsed upon refinancing of the debt (discussed below).

In September 2024, we entered into an amendment to the Original Loan Agreement (the "Amendment" and the Original Loan Agreement, as amended by the Amendment, the "Loan Agreement") increasing the maximum aggregate principal amount in delayed-draw term loans to $150.0 million (the "Term Loan") from $100.0 million. The Loan Agreement consists of (i) a first tranche of $70.0 million, of which $35.0 million was funded at closing (including the refinancing of the existing $25.0 million principal balance outstanding) and of which an additional $35.0 million is available through June 30, 2025, (ii) a second tranche of $30.0 million available to be funded upon the achievement of a specific clinical development milestone through December 31, 2025, and (iii) a third tranche of up to $50.0 million upon our request, subject to review by the Lenders of certain information from us and discretionary approval by the Lenders. We have not drawn any additional advances under the Loan Agreement since the September 2024 refinancing.

Funding Requirements

Our primary use of cash is to fund operating expenses, which consist primarily of research and development and manufacturing expenditures related to our lead product candidate, pegozafermin. We plan to increase our research and development expenses 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 current operating plan, we expect our existing cash, cash equivalents and marketable securities of $440.0 million as of December 31, 2024, supplemented by $269.9 million in net proceeds from our February 2025 equity offering, will be sufficient to fund our operations for a period of at least one year following the filing of this Form 10-K. 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 pegozafermin 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 pegozafermin 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;
- the cost of preparing, filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights; and
- the cost overruns under the Collaboration Agreement if the actual costs of the Production Facility are greater than the estimated budget.

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,	
	2024	2023
Net cash (used in) provided by:		
Operating activities	$ (367,823)	$ (129,186)
Investing activities	(40,864)	(123,019)
Financing activities	218,586	513,111
Net change in cash and cash equivalents	$ (190,101)	$ 260,906

Operating Activities

For the year ended December 31, 2024, net cash used in operating activities of $367.8 million reflects a net loss of $367.1 million and a net change of $14.5 million in operating assets and liabilities, partially offset by aggregate noncash charges of $13.8 million. The net loss was driven by milestone payments of $121.5 million (net of applicable value-added tax) made to our contract manufacturing partner, BiBo, under the Collaboration Agreement to secure manufacturing capacity to produce pegozafermin for our commercial needs. Noncash charges primarily included stock-based compensation expense of $20.6 million, a loss on extinguishment of debt of $1.5 million related to the refinancing of our term loan, noncash operating lease expense of $0.7 million and amortization of debt discount and accretion of deferred debt costs of $0.8 million, offset in part by net accretion of discounts on marketable securities of $10.0 million. The net change in operating assets and liabilities used cash of $14.5 million and was primarily due to an increase in prepaid and other assets of $21.7 million as we made prepayments related to the initiation and continuation of our Phase 3 clinical trials, and a decrease in lease liabilities of $0.5 million,

partially offset by a net increase in accounts payable and accrued expenses of $7.0 million driven by timing of payments made and an increase in services rendered by contract research organizations and contract manufacturing organizations in connection with the Phase 3 clinical trials.

For the year ended December 31, 2023, net cash used in operating activities of $129.2 million reflects a net loss of $142.2 million, partially offset by aggregate non-cash charges of $12.3 million and a net change of $0.7 million in our net operating assets and liabilities. The change in our operating assets and liabilities was primarily due to a net increase in accounts payable and accrued expenses of $4.0 million due to the timing of payments to vendors and a $3.7 million increase in other non-current liabilities related to tax accruals, offset in part by an increase in prepaid and other assets of $6.9 million related to our clinical trials, contract manufacturing and scale-up activities. Non-cash charges primarily included stock-based compensation expense of $16.1 million, a loss on debt extinguishment of $1.2 million related to our prior term loan, amortization of debt discount and accretion of the end of term fee related to our term loan facility of $0.9 million, offset in part by net accretion of discounts on marketable securities of $6.2 million.

Investing Activities

For the year ended December 31, 2024, net cash used in investing activities was $40.9 million, which consisted of $376.1 million in purchases of marketable securities, offset in part by $335.2 million in proceeds from sales and maturities of marketable securities.

For the year ended December 31, 2023, net cash used in investing activities was $123.0 million, which consisted of $341.1 million in purchases of marketable securities, offset in part by $218.1 million in proceeds from sales and maturities of marketable securities.

Financing Activities

For the year ended December 31, 2024, net cash provided by financing activities was $218.6 million, which primarily consisted of net proceeds of $136.3 million from the sale of common stock in public offerings, proceeds of $54.2 million from the exercise of common stock warrants, net proceeds of $21.0 million pursuant to the sale of our common stock under our 2023 ATM Facility, net proceeds of $9.3 million from borrowings under the Loan Agreement and proceeds of $0.6 million from employee stock plans. Partially offsetting these inflows were $2.9 million in cash outflows. This amount primarily reflects payments for employee withholding taxes associated with the net share settlement of restricted stock units. Additionally, a portion of these payments related to payments of deferred offering costs.

For the year ended December 31, 2023, net cash provided by financing activities was $513.1 million, which primarily consisted of net proceeds of $458.8 million from the sale of common stock in public offerings, net proceeds of $37.1 million pursuant to the sale of our common stock under our 2021 ATM Facility and 2023 ATM Facility, net proceeds of $24.4 million from borrowings under a term loan, proceeds of $15.6 million from the exercise of warrants and proceeds of $0.9 million from employee stock plans. This was offset in part by the repayment in full of $21.4 million on a prior term loan, including end of term and prepayment fees, and payments for taxes of $2.3 million related to net share settlement upon vesting of restricted stock units.

Contractual Obligations and Commitments

Our cash requirements greater than one year related to contractual obligations and commitments include the following:

Debt Obligations

As of December 31, 2024, the principal amount under our Loan Agreement was $35.0 million, which is scheduled to mature on October 1, 2028. The loan provides for interest-only payments until January 1, 2027, which can be extended to January 1, 2028 upon achievement of a clinical milestone. For additional information regarding the terms of the debt and interest payable, see Note 6 to our consolidated financial statements under Part II, Item 8 of this Annual Report on Form 10-K.

Asset Transfer and License Agreement with Teva Pharmaceutical Industries Ltd.

In April 2018, we concurrently entered into two Asset Transfer and License Agreements with Teva Pharmaceutical Industries Ltd ("Teva") under which we acquired certain patents and intellectual property relating to two programs: (1) Teva's glycoPEGylated FGF21 program, including the compound TEV-47948 (pegozafermin), a glycoPEGylated long-acting FGF21 (the "FGF21 Agreement") and (2) Teva's development program of small molecule inhibitors of Fatty Acid Synthase (the "FASN Agreement" and together with the FGF21 Agreement, the "Teva Agreements"). In the fourth quarter of 2024, we returned to Teva all rights associated with the program under the FASN Agreement. We did not develop any product candidates under the FASN Agreement. Pursuant to the Teva Agreements, we paid Teva an initial nonrefundable upfront payment of $6.0 million. Under the FGF21 Agreement, we are required to pay Teva $2.5 million upon the achievement of a specified clinical development milestone (payable once, upon the first time such milestone is achieved) 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 on all products containing pegozafermin. In the fourth quarter of 2023, we made a $2.5 million milestone payment to Teva following the achievement of a clinical development milestone under the FGF21 program in SHTG. As of December 31, 2024, the timing and likelihood of achieving any remaining milestones under the FGF21 Agreement are uncertain.

The FGF21 Agreement can be terminated (i) by us without cause upon 120 days' written notice to Teva, (ii) by either party, if the other party materially breaches any of its obligations under the agreement 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 their glycoPEGylated FGF21 program in the event we, or any of our affiliates or sublicensees, challenges any of the Teva patents licensed to us, and the challenge is not withdrawn within 30 days of written notice from Teva.

Production Facility Funding Commitments

In April 2024, we entered into the Collaboration Agreement, pursuant to which BiBo will construct the Production Facility. Under the Collaboration Agreement, we are required to pay BiBo an aggregate of $135.0 million (exclusive of applicable value-added tax) toward the construction of the Production Facility (collectively, the "Payment"), of which $121.5 million (net of applicable value-added tax) in milestone payments were paid during the year ended December 31, 2024. The remaining $13.5 million will become payable upon achievement of certain specified milestones. If the actual costs of the Production Facility are substantially greater than the estimated budget, the parties will negotiate a means of allocating such cost overruns.

Other Contractual Obligations and Commitments

As of December 31, 2024, our lease for our corporate headquarters represents substantially all of operating lease obligations and undiscounted future minimum lease payments of $2.1 million remain on our leases as of that date.

In addition, we enter into agreements in the normal course of business with contract research organizations, contract manufacturing organizations and other vendors for research and development services. Such agreements generally provide for termination upon written notice but obligate us to reimburse vendors for any time or costs incurred through the date of termination.

Critical Accounting 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. 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 or for which we have not received vendor statements 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 progress of work completed, including patient enrollment levels. 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.

Stock-Based Compensation

We utilize stock options, restricted stock units ("RSUs") and performance stock units ("PSUs") for equity compensation. We measure compensation related to equity awards granted to employees, directors, and non-employee service providers based on estimated fair values and recognize stock-based compensation over the requisite service period. We recognize forfeitures as they occur.

We estimate the fair value of stock option awards on the date of grant, and the resulting stock-based compensation, using the Black-Scholes option-pricing model. We recognize compensation for stock option awards, including awards with graded-vesting, on a straight-line basis over the requisite service period.

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 equity awards. These assumptions include:

- Expected volatility—We have a limited trading history for our common stock. As a result, we estimate the expected volatility based on a combination of our own historical stock price volatility and that of a publicly traded set of peer companies such that the time period over which historical volatility data used is at least equal to the expected term of the option award. The peer companies were chosen based on their similar size, stage in the life cycle, or area of specialty. We apply judgment in selecting a peer group as each of the peers are engaged in varied research and development activities, the timing and progress of which differ within the peer group.

- 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 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 stock options evenly over the period when the stock options are vested and ending on the date when the stock options would expire. The expected option term for options granted to non-employees is estimated on a grant-by-grant basis.

- Risk-free interest rate—The risk-free interest rate is based on the U.S. Treasury zero coupon bonds in effect on the grant date for periods with an equivalent expected term as the option.

- Expected dividend—We have never paid dividends and have no foreseeable plans to pay dividends on our shares of common stock. Therefore, we use an expected dividend of zero.

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

The grant date fair value of RSUs and PSUs are based on the closing price of our common stock on the date of grant. RSUs are service-based awards and are recognized over the requisite service period on a straight-line basis. Compensation expense for PSUs is recognized over the estimated service period for each tranche of an award (the accelerated attribution method) when its performance condition is deemed probable of achievement. For PSUs containing performance conditions which were not deemed probable of achievement, no stock compensation expense is recognized. Additionally, at each reporting period, we evaluate the probable outcome of the performance conditions and as applicable, recognize the cumulative effect of the change in estimate in the period of the change.

Income Taxes

Deferred tax assets and liabilities are recognized for the expected tax consequences of temporary differences between the tax bases of assets and liabilities and their reported amounts using enacted tax rates in effect for the year the differences are expected to reverse. In evaluating our ability to recover our deferred tax assets, we consider all available positive and negative evidence, including our past operating results, the existence of cumulative losses in past fiscal years, and our forecast of future taxable income in the jurisdictions in which we have operations.

We have established a valuation allowance on our U.S. deferred tax assets because realization of these tax benefits through future taxable income does not meet the more-likely-than-not threshold. We intend to maintain the valuation allowances until sufficient positive evidence exists to support the reversal of the valuation allowances.

The calculation of our tax liabilities involves dealing with uncertainties in the application of complex tax laws. Our estimate for the potential outcome of any uncertain tax issue is based on the detailed facts and circumstances of each issue. For example, in December 2023, we received a primary assessment from the Israeli Tax Authorities ("ITA") related to our 2019 reorganization and intercompany transaction to license the intellectual property rights from our Israeli subsidiary to our U.S. entity. The ITA has alleged that the transaction is deemed to be a sale of intellectual property rights. We are appealing the tax assessment and intend to continue to challenge the ITA's position. We believe our accruals for unrecognized tax benefits as of December 31, 2024 are adequate. However, it is possible that the final resolution of this matter could have a material impact on our consolidated financial statements. See further discussion in Note 9 to our consolidated financial statements appearing under Part II, Item 8 of this Annual Report on Form 10-K.

We recognize liabilities for uncertain tax positions based on a two-step process. The first step is to evaluate the tax position for recognition by determining if the weight of available evidence indicates that it is more likely than not that the position will be sustained on audit, including resolution of related appeals or litigation processes, if any. The second step requires us to estimate and measure the tax benefit as the largest amount that is more than 50% likely to be realized upon ultimate settlement. It is inherently difficult and subjective to estimate such amounts, as this requires us to determine the probability of various possible outcomes. We re-evaluate these uncertain tax positions on a quarterly basis. This evaluation is based on factors including, but not limited to, changes in facts or circumstances, changes in tax law, effectively settled issues under audit, and new audit activity. Such a change in recognition or measurement would result in the recognition of a tax benefit or an additional charge to income tax expense in the period of change.

Recent Accounting Pronouncements

See Note 2 to our consolidated financial statements appearing under Part II, Item 8 of this Annual Report on Form 10-K 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.

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

Interest Rate Risk

As of December 31, 2024, we had cash, cash equivalents and marketable securities of $440.0 million. We invest our excess cash primarily in money market funds and certificates of deposit, securities issued by the U.S. government and its agencies, corporate debt securities and commercial paper. We place our investments with high-quality credit issuers and, by policy, limit the amount of credit exposure to any one issuer. A portion of our investments consisting of interest-bearing securities are subject to interest rate risk and could decline in value due to a rise in interest rates. The portfolio includes cash equivalents and marketable securities with active secondary or resale markets to ensure portfolio liquidity. Due to the conservative nature of these instruments and the short-term maturities of our investments, we do not believe that a change in market interest rates would have a significant negative impact on the value of our investment portfolio except for reduced income in a low interest rate environment.

As of December 31, 2024, the aggregate outstanding principal balance under our term loan facility was $35.0 million. The term loan has a variable interest rate calculated by reference to the Prime Rate and matures on October 1, 2028. We carry these instruments at face value, less unamortized discounts and issuance costs, on our accompanying consolidated balance sheets. Based on the outstanding balance at December 31, 2024, an immediate 10% change in interest rates would not have a material effect on the fair value of our term loan, and would not have a significant impact on our financial statements as we do not record debt at fair value.

Foreign Exchange Risk

As a result of our operations in Israel, we have exposure to fluctuations in exchange rates from transactions that are denominated in the New Israeli Shekel ("NIS"). The functional currency of our subsidiary in Israel is the U.S. Dollar. Our exposure arises primarily from cash, accounts payable and accrued expenses denominated in NIS. We have not hedged our foreign currency since the exposure has not been material to our historical operating results. Based on our foreign currency exchange rate exposures at December 31, 2024, a hypothetical 10% adverse fluctuation in the average exchange rate of the NIS would not have had a material impact on our consolidated financial statements. We will continue to monitor and evaluate our exposure to foreign exchange risk as a result of entering into transactions denominated in currencies other than the U.S. Dollar.

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 Board of Directors
89bio, Inc.:

Opinions on the Consolidated Financial Statements and Internal Control Over Financial Reporting

We have audited the accompanying consolidated balance sheets of 89bio, Inc. and subsidiaries (the Company) as of December 31, 2024 and 2023, the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows for each of the years in the three-year period ended December 31, 2024, and the related notes (collectively, the consolidated financial statements). We also have audited the Company's internal control over financial reporting as of December 31, 2024, based on criteria established in *Internal Control – Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission.

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2024 and 2023, and the results of its operations and its cash flows for each of the years in the three-year period ended December 31, 2024, in conformity with U.S. generally accepted accounting principles. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2024 based on criteria established in *Internal Control – Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission.

Basis for Opinions

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

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

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

Definition and Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance

with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

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

Critical Audit Matters

Critical audit matters are matters arising from the current period audit of the consolidated financial statements that were communicated or required to be communicated to the audit committee and that: (1) relate to accounts or disclosures that are material to the consolidated financial statements and (2) involved our especially challenging, subjective, or complex judgments. We determined that there are no critical audit matters.

/s/ KPMG LLP

We have served as the Company's auditor since 2020.

San Francisco, California
February 27, 2025

89bio, Inc.
Consolidated Balance Sheets
(In thousands, except share and par value amounts)

	As of December 31,	
	2024	2023
Assets		
Current assets:		
Cash and cash equivalents	$ 126,060	$ 316,161
Marketable securities	313,895	262,709
Prepaid and other current assets	36,495	14,664
Total current assets	476,450	593,534
Operating lease right-of-use assets	1,572	2,293
Property and equipment, net	23	46
Other assets	640	396
Total assets	$ 478,685	$ 596,269
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 15,382	$ 8,585
Accrued expenses	20,020	20,530
Operating lease liabilities, current	727	496
Total current liabilities	36,129	29,611
Operating lease liabilities, noncurrent	1,090	1,817
Warrant liability	516	—
Term loan, noncurrent, net	35,732	24,795
Other noncurrent liabilities	4,429	3,740
Total liabilities	77,896	59,963
Commitments and contingencies (Note 5)		
Stockholders' equity:		
Preferred stock, $0.001 par value: 10,000,000 shares authorized; none issued and outstanding	—	—
Common stock, $0.001 par value: 200,000,000 shares authorized; 119,849,436 and 93,269,377 shares issued and outstanding as of December 31, 2024 and 2023, respectively	120	93
Additional paid-in capital	1,224,617	993,455
Accumulated other comprehensive income	563	190
Accumulated deficit	(824,511)	(457,432)
Total stockholders' equity	400,789	536,306
Total liabilities and stockholders' equity	$ 478,685	$ 596,269

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,		
	2024	2023	2022
Operating expenses:			
Research and development	$ 345,037	$ 122,230	$ 80,796
General and administrative	39,619	28,974	21,453
Total operating expenses	384,656	151,204	102,249
Loss from operations	(384,656)	(151,204)	(102,249)
Interest expense	(5,290)	(4,794)	(1,922)
Interest income and other, net	23,559	17,676	2,164
Net loss before income tax	(366,387)	(138,322)	(102,007)
Income tax expense	(692)	(3,867)	(19)
Net loss	$ (367,079)	$ (142,189)	$ (102,026)
Other comprehensive income (loss):			
Unrealized gain (loss) on marketable securities	364	547	(299)
Foreign currency translation adjustments	9	(7)	13
Total other comprehensive income (loss)	$ 373	$ 540	$ (286)
Comprehensive loss	$ (366,706)	$ (141,649)	$ (102,312)
Net loss per share, basic and diluted	$ (3.51)	$ (2.00)	$ (2.93)
Weighted-average shares used to compute net loss per share, basic and diluted	104,714,613	71,172,870	34,806,349

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

89bio, Inc.
Consolidated Statements of Stockholders' Equity
(In thousands, except share amounts)

	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive (Loss) Income	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amounts				
Balance as of December 31, 2021	20,317,204	$ 20	$ 339,218	$ (64)	$ (213,217)	$ 125,957
Issuance of common stock and warrants in public offering, net of issuance costs	18,675,466	20	88,219	—	—	88,239
Issuance of common stock in at-the-market public offering, net of issuance costs	3,948,611	4	28,449	—	—	28,453
Issuance of common stock upon exercise of common stock warrants	4,202,499	4	1,078	—	—	1,082
Issuance of common stock upon cashless exercise of pre-funded warrants	3,143,682	3	(3)	—	—	—
Issuance of common stock upon exercise of stock options	151,061	—	305	—	—	305
Issuance of common stock under employee stock purchase plan	18,364	—	50	—	—	50
Issuance of common stock upon vesting of restricted stock units, net of tax withholding for net share settlement	103,703	—	(298)	—	—	(298)
Stock-based compensation	—	—	10,356	—	—	10,356
Net loss	—	—	—	—	(102,026)	(102,026)
Other comprehensive loss	—	—	—	(286)	—	(286)
Balance as of December 31, 2022	50,560,590	$ 51	$ 467,374	$ (350)	$ (315,243)	$ 151,832
Issuance of common stock and pre-funded warrants in public offering, net of issuance costs	37,029,105	37	458,553	—	—	458,590
Issuance of common stock in at-the-market public offerings, net of issuance costs	2,168,539	2	37,087	—	—	37,089
Issuance of common stock warrants related to term loan facility	—	—	482	—	—	482
Issuance of common stock upon exercise of common stock warrants	2,927,570	3	15,587	—	—	15,590
Issuance of common stock upon exercise of stock options	247,162	—	730	—	—	730
Issuance of common stock upon vesting of restricted stock units, net of tax withholding for net share settlement	309,194	—	(2,732)	—	—	(2,732)
Issuance of common stock under employee stock purchase plan	27,217	—	268	—	—	268
Stock-based compensation	—	—	16,106	—	—	16,106
Net loss	—	—	—	—	(142,189)	(142,189)
Other comprehensive income	—	—	—	540	—	540
Balance as of December 31, 2023	93,269,377	$ 93	$ 993,455	$ 190	$ (457,432)	$ 536,306
Issuance of common stock and pre-funded warrants in public offering, net of issuance costs	13,661,764	14	136,269	—	—	136,283
Issuance of common stock in at-the-market public offerings, net of issuance costs	1,396,888	2	21,047	—	—	21,049
Issuance of common stock warrants related to amended term loan facility	—	—	608	—	—	608
Issuance of common stock upon exercise of common stock warrants	10,179,789	10	54,197	—	—	54,207
Issuance of common stock upon cashless exercise of pre-funded warrants	799,906	1	(1)	—	—	—
Issuance of common stock upon exercise of stock options	76,003	—	242	—	—	242
Issuance of common stock upon vesting of restricted stock units, net of tax withholding for net share settlement	412,558	—	(2,190)	—	—	(2,190)
Issuance of common stock under employee stock purchase plan	53,151	—	356	—	—	356
Stock-based compensation	—	—	20,634	—	—	20,634
Net loss	—	—	—	—	(367,079)	(367,079)
Other comprehensive income	—	—	—	373	—	373
Balance as of December 31, 2024	119,849,436	$ 120	$ 1,224,617	$ 563	$ (824,511)	$ 400,789

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,		
	2024	2023	2022
Cash flows from operating activities:			
Net loss	$ (367,079)	$ (142,189)	$ (102,026)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation	20,634	16,106	10,356
Accretion of discounts on marketable securities, net of amortization of premiums	(9,972)	(6,242)	(980)
Amortization of debt discount and accretion of deferred debt costs	831	874	764
Loss on extinguishment of debt	1,503	1,208	—
Noncash operating lease expense	721	223	175
Depreciation	38	50	65
Other	29	127	—
Changes in operating assets and liabilities:			
Prepaid and other assets	(21,726)	(6,921)	3,331
Accounts payable	7,058	(3,917)	5,659
Accrued expenses	(53)	7,876	1,750
Operating lease liabilities	(496)	(121)	(184)
Other noncurrent liabilities	689	3,740	—
Net cash used in operating activities	(367,823)	(129,186)	(81,090)
Cash flows from investing activities:			
Proceeds from sales and maturities of marketable securities	335,225	218,133	118,760
Purchases of marketable securities	(376,074)	(341,148)	(152,696)
Purchases of property and equipment	(15)	(4)	(7)
Net cash used in investing activities	(40,864)	(123,019)	(33,943)
Cash flows from financing activities:			
Proceeds from issuance of common stock and warrants in public offerings, net of issuance costs	136,283	458,843	88,239
Proceeds from issuance of common stock in at-the-market public offerings, net of issuance costs	21,049	37,089	28,453
Proceeds from term loan facility, net of issuance costs	9,349	24,363	—
Proceeds from issuance of common stock upon exercise of common stock warrants	54,207	15,590	1,082
Proceeds from issuance of common stock upon exercise of stock options	242	633	305
Proceeds from issuance of common stock under employee stock purchase plan	356	268	50
Payments of deferred offering costs	(253)	—	—
Payments for taxes related to net share settlement upon vesting of restricted stock units	(2,647)	(2,275)	(298)
Repayment of term loan	—	(21,400)	—
Net cash provided by financing activities	218,586	513,111	117,831
Net change in cash and cash equivalents	(190,101)	260,906	2,798
Cash and cash equivalents:			
Beginning of period	316,161	55,255	52,457
End of period	$ 126,060	$ 316,161	$ 55,255
Supplemental disclosures of cash information:			
Cash paid for interest	$ 3,135	$ 2,593	$ 1,076
Cash paid for amounts included in the measurement of lease liabilities	$ 774	$ 185	$ 234
Supplemental disclosures of noncash information:			
Unpaid offering costs included in accrued expenses	$ —	$ 253	$ —
Right-of-use assets obtained in exchange for operating lease liabilities	$ —	$ 2,080	$ —
Remeasurement of lease liability and right of use asset in connection with lease modification	$ —	$ —	$ 338
Issuance of common stock warrants in connection with term loans	$ 608	$ 482	$ —

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

89bio, Inc.
Notes to Consolidated Financial Statements

1. Organization and Basis of Presentation

Description of Business

89bio, Inc. (including its consolidated subsidiaries, also referred to as "89bio," the "company," "we," "our" or "us") is 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, pegozafermin, a specifically engineered glycoPEGylated analog of fibroblast growth factor 21 ("FGF21"), is currently being developed for the treatment of metabolic dysfunction-associated steatohepatitis ("MASH"), previously known as nonalcoholic steatohepatitis, and for the treatment of severe hypertriglyceridemia ("SHTG").

89bio was formed as a Delaware corporation in June 2019 to carry on the business of 89Bio Ltd., which was incorporated in Israel in January 2018.

Liquidity

We have incurred significant losses and negative cash flows from operations since inception and had an accumulated deficit of $824.5 million as of December 31, 2024. We have historically financed our operations primarily through the sale of equity securities, including warrants, and from borrowings under term loan facilities. To date, none of our product candidates have been approved for sale, and we have not generated any revenue from commercial products. We expect operating losses to continue and increase for the foreseeable future as we progress our clinical development activities for our product candidates.

We believe our existing cash, cash equivalents and marketable securities of $440.0 million as of December 31, 2024, supplemented by $269.9 million in net proceeds from our February 2025 equity offering, will be sufficient to fund our planned operating expense and capital expenditure requirements for a period of at least one year from the issuance date of these consolidated financial statements.

2. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States ("U.S. GAAP"). Any reference in these notes to applicable guidance is meant to refer to the authoritative U.S. GAAP as found in the Accounting Standards Codification ("ASC") and Accounting Standards Updates ("ASU") of the Financial Accounting Standards Board ("FASB").

Principles of Consolidation

The accompanying consolidated financial statements include the accounts of 89bio and our wholly-owned subsidiaries. All intercompany balances and transactions have been eliminated in consolidation.

Use of Estimates

The preparation of consolidated financial statements in conformity with U.S. GAAP requires us 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 accruals for uncertain tax positions, accrued research and development expenses and the valuation of stock options. We evaluate our 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.

Foreign Currencies

We engage in foreign-currency-denominated transactions with certain vendors, as well as between subsidiaries with different functional currencies. Our subsidiary in Israel uses the U.S. dollar as its functional currency for financial reporting. Gains and losses from foreign-currency-denominated transactions, primarily denominated in

New Israeli Shekels, were not material for all periods presented and are reflected in the consolidated statements of operations and comprehensive loss as a component of interest income and other, net. Our subsidiary in Lithuania uses the Euro as its functional currency for financial reporting. The re-measurement from Euros to U.S. dollars results in translation gain and loss adjustments, which are included in the consolidated balance sheets as part of accumulated other comprehensive income.

Fair Value Measurements

Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability (an exit price) in an orderly transaction between market participants at the reporting date. 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; and

Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

Assets and Liabilities Measured at Fair Value on a Recurring Basis

Financial instruments measured and recorded at fair value on a recurring basis consist of cash equivalents and marketable securities and common stock warrants issued in connection with a term loan facility that do not meet all of the criteria for equity classification.

Financial Instruments Not Carried at Fair Value

Our financial instruments, including cash, other current assets, accounts payable and accrued expenses are carried at cost which approximates their fair value because of the short-term nature of these financial instruments. The fair value of our term loan approximates its carrying value, or amortized cost, due to the prevailing market rates of interest it bears.

Concentrations of Credit Risk

Financial instruments that potentially subject us to concentrations of credit risk consist primarily of cash, cash equivalents and marketable securities. Bank deposits are held by accredited financial institutions and these deposits may at times be in excess of insured limits. We limit our credit risk associated with cash and cash equivalents by placing them with financial institutions that we believe are of high quality. We have not experienced any losses on our deposits of cash or cash equivalents. We have established guidelines relative to diversification and maturities to maintain safety and liquidity and limit amounts invested in marketable securities by credit rating, maturity, industry group, investment type and issuer, except for securities issued by the U.S. government. As of December 31, 2024, we do not believe a significant risk of loss from a concentration of credit risk exists with respect to our marketable securities.

Other Risks and Uncertainties

Our future results of operations involve a number of other risks and uncertainties. Factors that could affect our future operating results and cause actual results to vary materially from expectations include, but are not limited to, our early stages of clinical drug development; our ability to advance product candidates into, and successfully complete, clinical trials on the timelines we project; our ability to adequately demonstrate sufficient safety and efficacy of our product candidates; our ability to enroll patients in our ongoing and future clinical trials; our ability to successfully manufacture and supply our product candidates for clinical trials; our ability to obtain additional capital to finance our operations; uncertainties related to the projections of the size of patient populations suffering from the diseases we are targeting; our ability to obtain, maintain, and protect our intellectual property rights;

developments relating to our competitors and our industry, including competing product candidates and therapies; general economic and market conditions; and other risks and uncertainties.

Our 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 we are denied approval, approval is delayed or we are unable to maintain approval for any product candidate, it could have a materially adverse impact on us.

Segment Information

Operating segments are defined as components of an enterprise that have the following characteristics: (i) they engage in business activities from which they may earn revenue and incur expense, (ii) their operating results are regularly reviewed by the chief operating decision maker ("CODM") for resource allocation decisions and performance assessment, and (iii) their discrete financial information is available. Our CODM is our Chief Executive Officer, who manages and allocates resources to our operations on a consolidated basis. We operate as one segment and our operations are focused on the development and commercialization of innovative therapies for the treatment of liver and cardio-metabolic diseases. Segment information is further described in Note 11.

Cash and Cash Equivalents

We consider all highly-liquid investments purchased with original maturities of three months or less from the purchase date to be cash equivalents. Cash equivalents primarily consist of amounts invested in money market funds, commercial paper and U.S. government treasury securities and are carried at fair value.

Marketable Securities

We invest our excess cash in marketable securities with high credit ratings including money market funds, commercial paper, securities issued by the U.S. government and its agencies and corporate debt securities. We account for all marketable securities as available-for-sale, as the sale of such securities may be required prior to maturity. These marketable securities are carried at fair value, with unrealized gains and losses reported as accumulated other comprehensive income (loss) until realized. The cost of debt securities is adjusted for accretion of premiums and amortization of discounts to maturity. Such amortization and accretion, as well as interest and dividends, are included in interest income and other, net. Realized gains and losses from the sale of available-for-sale securities, if any, are determined on a specific identification basis and are also included in interest income and other, net. We classify our marketable securities as current assets, which reflects our intention to use the proceeds from sales of these securities to fund our operations, as necessary, even though the stated maturity date may be one year or more beyond the current balance sheet date.

We periodically assess our available-for-sale marketable securities for impairment. For marketable securities in an unrealized loss position, this assessment first takes into account our intent to sell, or whether it is more likely than not that we will be required to sell the security before recovery of its amortized cost basis. If either of these criteria are met, the marketable security's amortized cost basis is written down to fair value through interest income and other, net. For marketable securities in an unrealized loss position that do not meet the aforementioned criteria, we assess whether the decline in fair value has resulted from credit losses or other factors. In making this assessment, we consider the extent to which fair value is less than amortized cost, any changes to the rating of the security by a rating agency, and any adverse conditions specifically related to the security, among other factors. If this assessment indicates that a credit loss may exist, the present value of cash flows expected to be collected from the security are compared to the amortized cost basis of the security. If the present value of cash flows expected to be collected is less than the amortized cost basis, a credit loss exists and an allowance for credit losses will be recorded in interest income and other, net, limited by the amount that the fair value is less than the amortized cost basis. Impairment not recorded through an allowance for credit losses is recognized in other comprehensive loss. Changes in the allowance for credit losses are recorded as provision for (or reversal of) credit loss expense. Losses are charged against the allowance when we believe the uncollectability of an available-for-sale security is confirmed or when either of the criteria regarding intent or requirement to sell is met. These changes are recorded in interest income and other, net. To date, we have not experienced any credit-related losses on our marketable securities.

Leases

We have noncancellable operating leases for office space. We determine whether a contract is or contains a lease at contract inception based on the presence of identified assets and our right to obtain substantially all the economic benefit from or to direct the use of such assets. When we determine a lease exists, we record a right-of-use ("ROU") asset and corresponding lease liability on our consolidated balance sheet. ROU assets represent our right to use an underlying asset for the lease term. Lease liabilities represent our obligation to make lease payments arising from the lease. ROU assets are recognized at the lease commencement date at the value of the lease liability and are adjusted for any prepayments, lease incentives received, and initial direct costs incurred. Lease liabilities are recognized at the lease commencement date based on the present value of remaining lease payments over the lease term. The present value of lease payments is determined by using the interest rate implicit in the lease, if that rate is readily determinable; otherwise, we use our estimated collateralized incremental borrowing rate that we would pay for a similar amount and term. Lease liabilities are subsequently measured at amortized cost using the effective-interest method. Our lease terms include options to extend or terminate the lease when it is reasonably certain that we will exercise that option. We do not record lease contracts with a term of 12 months or less on our consolidated balance sheets. We do not have any material short-term leases.

When our real estate lease arrangements include lease and non-lease components (for example, common area maintenance and other operating costs), we have applied the practical expedient to combine fixed payments for non-lease components with lease payments and account for them together as a single lease component, which increases assets and corresponding liabilities. Any variable payments are expensed as incurred and are not included in the operating lease asset and liability. Lease expense for an operating lease liability is recognized on a straight-line basis over the lease term, including any rent-free periods, and is included in operating expenses.

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 consolidated balance sheets and the resulting gains or losses are recorded in the consolidated statements of operations and comprehensive loss. Maintenance and repair costs are expensed as incurred.

Impairment of Long-Lived Assets

We periodically evaluate our long-lived assets, including property and equipment and ROU assets, 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, we reduce 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 impairment indicators for the periods presented.

Accrued Research and Development Expenses

We record 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 majority of these expenses are recorded based on invoices and statements received from these vendors. We also record these expenses based upon the estimated services provided but not yet invoiced. Liabilities associated with these expenses are included in accrued expenses in the consolidated balance sheets. These costs are recorded as research and development expenses.

In making these estimates of services provided but not yet invoiced or for which statements have not been received from vendors, we consider factors such as estimates of the progress of work completed in accordance with agreements established with our third-party service providers. As actual costs become known, we adjust our accrued expenses. We have not experienced any material differences between accrued costs and actual costs incurred. However, the status and timing of actual services performed may vary from our estimates, resulting in adjustments to expense in future periods. Changes in these estimates that result in material changes to our accrued expenses

could materially affect our results of operations. Contingent milestone payments, if any, are recognized when payment becomes probable and reasonably estimable, which is generally upon achievement of the milestone.

Warrants to Purchase Common Stock

Warrants to purchase common stock are classified as either a liability or equity. If the warrants are mandatorily redeemable, require settlement in cash or a variable number of shares, they are classified as a liability. If not classified as a liability under those criteria, we then assess whether the warrants may require cash settlement. Warrants that may require cash settlement are classified as liabilities, regardless of the likelihood of that settlement. Liability-classified warrants are measured at fair value, with changes in fair value recognized in the consolidated statements of operations and comprehensive loss as a gain or loss. If the warrants do not require liability classification under those criteria, and are indexed to our common stock, they are classified as equity. Equity-classified warrants are initially measured at fair value, with no subsequent changes in fair value recognized.

Research and Development Expenses

Research and development expenses are expensed as incurred and consist primarily of costs incurred for the development of our lead product candidate, pegozafermin. Research and development expenses consist primarily of external costs related to preclinical and clinical development and related supplies and personnel costs. Personnel costs consist of salaries, employee benefits and stock-based compensation for individuals involved in research and development efforts. Payments made to third parties under these arrangements in advance of the performance of the related services by the third parties are recorded as prepaid expenses until the services are rendered.

Payments associated with agreements to acquire licenses to develop, use, manufacture and commercialize products and purchases of pegozafermin from contract manufacturing organizations that have not reached technological feasibility and do not have alternate future commercial use are expensed as incurred. Where contingent milestone payments are due to third parties under license or other agreements, the milestone payment obligations are recognized as expense when achievement of the contingent milestone is probable, which is generally upon achievement of the milestone.

Stock-Based Compensation

We utilize stock options, restricted stock units ("RSUs") and performance stock units ("PSUs") for equity compensation. We measure equity awards made to employees, directors, and non-employee service providers based on estimated fair values and recognize stock-based compensation over the requisite service period. We account for forfeitures as they occur.

We estimate the fair value of stock option awards on the date of grant using a Black-Scholes option pricing model. We recognize compensation for stock option awards, including awards with graded-vesting, on a straight-line basis over the requisite service period.

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 dividend rate. These assumptions include:

- Expected volatility—We have a limited trading history for our common stock. As a result, we estimate expected volatility based on a combination of our own historical stock price volatility and that of a publicly traded set of peer companies such that the time period over which historical volatility data used is at least equal to the expected term of the option award. The peer companies were chosen based on their similar size, stage in the life cycle, or area of specialty.

- 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 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 stock options evenly over the period when the stock options are vested and ending on the date when the stock options would expire. The expected option term for options granted to non-employees is estimated on a grant-by-grant basis.

- Risk-free interest rate—The risk-free interest rate is based on the U.S. Treasury zero coupon bonds in effect on the grant date for periods with an equivalent expected term as the option.

- Expected dividend—We have never paid dividends and have no foreseeable plans to pay dividends on our shares of common stock. Therefore, an expected dividend of zero is used.

The grant date fair value of RSUs and PSUs are based on the closing price of our common stock on the date of grant. RSUs are service-based awards and are recognized over the requisite service period on a straight-line basis. Compensation expense for PSUs is recognized over the estimated service period for each tranche of an award (the accelerated attribution method) when its performance condition is deemed probable of achievement. For PSUs containing performance conditions which were not deemed probable of achievement, no stock compensation expense is recognized. Additionally, at each reporting period, we evaluate the probable outcome of the performance conditions and as applicable, recognize the cumulative effect of the change in estimate in the period of the change.

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. We have established full valuation allowances on our U.S. deferred tax assets because realization of these tax benefits through future taxable income is not more likely than not as of December 31, 2024 and 2023. We intend to maintain the valuation allowances until sufficient positive evidence exists to support the reversal of the valuation allowances.

The calculation of our accruals for tax contingencies involves dealing with uncertainties in the application of complex tax laws. Our estimates for the potential outcome of any uncertain tax issue are based on the detailed facts and circumstances of each issue. Resolution of these uncertainties in a manner inconsistent with our expectations could have a material impact on our results of operations and financial condition. We recognize liabilities for uncertain tax positions based on a two-step process. The first step is to evaluate the tax position for recognition by determining if the weight of available evidence indicates that it is more likely than not that the position will be sustained on audit, including resolution of related appeals or litigation processes, if any. The second step is to estimate and measure the tax benefit as the largest amount that is more than 50% likely of being realized upon ultimate settlement. It is inherently difficult and subjective to estimate such amounts, as this requires us to determine the probability of various possible outcomes. We reevaluate these uncertain tax positions on a quarterly basis. This evaluation is based on factors including, but not limited to, changes in facts or circumstances, changes in tax law, effectively settled issues under audit, and new audit activity. Based on new information becoming available, or other relevant developments occur, we adjust our accrued amounts accordingly. Any adjustment will impact income tax expense or benefit in the period in which such determination is made, and the adjustment could be material. Interest and penalties related to unrecognized tax benefits are included within income tax expense.

Basic and Diluted Net Loss per Share

Basic and diluted net loss per share is calculated based upon the weighted-average number of shares of common stock outstanding during the period. Shares of common stock that are potentially issuable for little or no cash consideration at issuance are included in the calculation of basic and diluted net loss per share, even if they are antidilutive.

During periods of income, participating securities are allocated a proportional share of income determined by dividing total weighted-average participating securities by the sum of the total weighted-average common shares and participating securities (the “two-class method”). Shares of our common stock warrants participate in any dividends that may be declared by us and are therefore considered to be participating securities. Participating securities have the effect of diluting both basic and diluted earnings per share during periods of income. During

periods of loss, no loss is allocated to participating securities since they have no contractual obligation to share in our losses. Diluted loss per share is computed after giving consideration to the dilutive effect of stock options, RSUs, PSUs and common stock warrants, except where such non-participating securities would be anti-dilutive. As we incurred net losses 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

Comprehensive loss is comprised of net loss and changes in unrealized gains or losses on marketable securities and foreign currency translation adjustments.

Recently Adopted Accounting Standards

In November 2023, the FASB issued ASU No. 2023-07, *Segment Reporting (Topic 280): Improvements to Reportable Segment Disclosures* ("ASU 2023-07"), which is intended to improve reportable segment disclosure requirements, primarily through enhanced disclosures about significant expenses. ASU 2023-07 requires disclosures to include significant segment expenses that are regularly provided to the CODM, a description of other segment items by reportable segment, and any additional measures of a segment's profit or loss used by the CODM when deciding how to allocate resources. The ASU also requires all annual disclosures required by Topic 280 to be included in interim periods. The ASU does not change how a public entity identifies its operating segments, aggregates them, or applies the quantitative thresholds to determine its reportable segments. We adopted this ASU for the annual period ended December 31, 2024 on a retrospective basis. While the adoption had no impact on our financial statements, additional required disclosures have been included in Note 11.

Recently Issued Accounting Pronouncements

In December 2023, the FASB issued ASU No. 2023-09, *Income Taxes (Topic 740): Improvements to Income Tax Disclosures* ("ASU 2023-09"), which requires companies to disclose, on an annual basis, specific categories in the effective tax rate reconciliation and provide additional information for reconciling items that meet a quantitative threshold. In addition, ASU 2023-09 requires companies to disclose additional information about income taxes paid. The ASU is effective for our annual periods beginning on January 1, 2025 and will be applied on a prospective basis with the option to apply the standard retrospectively. There will be no impact to our consolidated financial statements; however, there will be changes to our consolidated financial statement disclosures, primarily related to the effective tax rate reconciliation and cash paid for income taxes.

In November 2024, the FASB issued ASU No. 2024-03, *Income Statement-Reporting Comprehensive Income-Expense Disaggregation Disclosures (Subtopic 220-40): Disaggregation of Income Statement Expenses*, that will require entities to provide enhanced disclosures related to certain expense categories included in income statement captions. The ASU aims to increase transparency and provide investors with more detailed information about the nature of expenses reported on the face of the income statement. The standard does not change the requirements for the presentation of expenses on the face of the income statement. The ASU is effective for our annual reporting periods beginning January 1, 2027 and interim reporting periods beginning after January 1, 2028. Early adoption is permitted. We are currently evaluating the effect of adopting this new accounting guidance on our financial statement disclosures.

3. Fair Value Measurements

Assets Measured at Fair Value on a Recurring Basis

The following table presents our financial assets measured at fair value on a recurring basis by level within the fair value hierarchy as of December 31, 2024 (in thousands):

	Valuation Hierarchy	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Money market funds	Level 1	$ 22,645	$ —	$ —	$ 22,645
Commercial paper	Level 2	51,982	14	(5)	51,991
U.S. government bonds	Level 2	169,860	439	(29)	170,270
Agency bonds	Level 2	63,753	111	(5)	63,859
Corporate debt securities	Level 2	6,154	15	(3)	6,166
U.S. Treasury securities	Level 2	44,499	10	—	44,509
Agency discount securities	Level 2	18,940	2	—	18,942
Total cash equivalents and marketable securities		$ 377,833	$ 591	$ (42)	$ 378,382
Classified as:					
Cash equivalents					$ 64,487
Marketable securities					313,895
Total cash equivalents and marketable securities					$ 378,382

The following table presents our financial assets measured at fair value on a recurring basis by level within the fair value hierarchy as of December 31, 2023 (in thousands):

	Valuation Hierarchy	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Money market funds	Level 1	$ 493	$ —	$ —	$ 493
Commercial paper	Level 2	94,261	—	(55)	94,206
U.S. government bonds	Level 2	137,976	250	(142)	138,084
Agency bonds	Level 2	45,481	152	(44)	45,589
Corporate debt securities	Level 2	3,177	—	(12)	3,165
U.S. Treasury securities	Level 2	71,754	36	(1)	71,789
Agency discount securities	Level 2	7,975	1	—	7,976
Total cash equivalents and marketable securities		$ 361,117	$ 439	$ (254)	$ 361,302
Classified as:					
Cash equivalents					$ 98,593
Marketable securities					262,709
Total cash equivalents and marketable securities					$ 361,302

The valuation techniques used to measure the fair values of our Level 2 financial instruments, which generally have counterparties with high credit ratings, are based on quoted market prices when available. If quoted market prices are not available, the fair value for the security is estimated under the market or income approach using pricing models with market observable inputs.

The following table summarizes our cash equivalents and marketable securities by contractual maturity as of December 31, 2024 (in thousands):

Within one year	$ 351,711
After one year through two years	26,671
Total cash equivalents and marketable securities	$ 378,382

For the years ended December 31, 2024 and 2023, we did not recognize an allowance for credit-related losses for any of our investments.

Liabilities Measured at Fair Value on a Recurring Basis

Warrant Liability

As of December 31, 2024, our only financial liability measured at fair value on a recurring basis relates to warrants to purchase up to 311,996 shares of our common stock issued in connection with the Term Loan (See Note 6). The number of warrants that become exercisable is contingent on subsequent loan advances drawn by us under the Term Loan facility. As such, the warrants are not considered to be indexed to our own stock and were accounted for as a liability. We recorded the fair value of the warrants upon issuance using a probability-weighted scenario analysis with a Black-Scholes option-pricing model. We are required to revalue the warrants at each reporting date with any changes in fair value recorded on the consolidated statements of operations and comprehensive loss until the exercise contingencies are resolved. The valuation of the warrants is considered under Level 3 of the fair value hierarchy, taking into account the likelihood of the warrants becoming exercisable in addition to assumptions used in the Black-Scholes option-pricing model.

The reconciliation of our warrant liability measured at fair value on a recurring basis using unobservable inputs (Level 3) is as follows:

	Warrant Liability
Balance outstanding as of December 31, 2023	$ —
Issued in connection with Term Loan facility	487
Change in fair value	29
Balance outstanding as of December 31, 2024	$ 516

The warrants had a fair value of $0.5 million as of December 31, 2024, based on a Black-Scholes valuation with the following assumptions: risk-free interest rate of 4.6%, no dividends, expected volatility of 87.3% and expected term of 9.8 years.

4. Consolidated Balance Sheet Components

Prepaid and other current assets consist of the following as of the periods presented (in thousands):

	As of December 31,	
	2024	2023
Prepaid research and development	$ 32,550	$ 11,579
Prepaid taxes	368	614
Prepaid other	3,577	2,471
Total prepaid and other current assets	$ 36,495	$ 14,664

Accrued expenses consist of the following as of the periods presented (in thousands):

	As of December 31,	
	2024	2023
Accrued research and development expenses	$ 11,426	$ 13,017
Accrued employee and related expenses	6,872	6,248
Accrued professional and legal fees	1,680	1,110
Accrued other expenses	42	155
Total accrued expenses	$ 20,020	$ 20,530

5. Commitments and Contingencies

Leases

As of December 31, 2024, our lease for our corporate headquarters represents substantially all of operating lease obligations. In November 2023, we entered into a lease ("HQ Lease") with respect to approximately 17,616 square feet of office space in San Francisco, California for a lease term commencing in the fourth quarter of 2023 and ending in March 2027. The HQ Lease does not provide for any extension or renewal options. The HQ Lease includes an abatement period during which we were not required to remit monthly rent payments until April 2024 and has escalating rent payments during the lease term. Additionally, the scheduled lease payments also include our proportionate share of certain operating expenses. All scheduled lease payments have been included in the measurement of right-of-use assets and lease liabilities in accordance with our accounting policy election to account for lease and non-lease components together as a single lease component.

Our lease for approximately 3,600 square feet of additional office space in San Francisco under a non-cancelable operating lease expired in January 2025.

For the years ended December 31, 2024, 2023 and 2022, lease expense was $1.0 million, $0.3 million and $0.2 million, respectively. Variable lease payments for the same periods were not material. As of December 31, 2024, the weighted-average remaining lease term was 2.2 years and the weighted-average incremental borrowing rate used to determine operating lease liabilities was 13.4%.

As of December 31, 2024, the undiscounted future minimum lease payments due under non-cancellable operating leases were as follows (in thousands):

2025	$	917
2026		937
2027		240
Total undiscounted future minimum lease payments	$	2,094
Less: imputed interest		(277)
Present value of operating lease liabilities	$	1,817

Asset Transfer and License Agreement with Teva Pharmaceutical Industries Ltd

In April 2018, we concurrently entered into two Asset Transfer and License Agreements with Teva Pharmaceutical Industries Ltd ("Teva") under which we acquired certain patents and intellectual property relating to two programs: (1) Teva's glycoPEGylated FGF21 program, including the compound TEV-47948 (pegozafermin), a glycoPEGylated long-acting FGF21 (the "FGF21 Agreement") and (2) Teva's development program of small molecule inhibitors of Fatty Acid Synthase (the "FASN Agreement" and together with the FGF21 Agreement, the "Teva Agreements"). In the fourth quarter of 2024, we returned to Teva all rights associated with the program under the FASN Agreement. We did not develop any product candidates under the FASN Agreement. Pursuant to the Teva Agreements, we paid Teva an initial nonrefundable upfront payment of $6.0 million. Under the FGF21 Agreement, we are required to pay Teva $2.5 million upon the achievement of a specified clinical development milestone (payable once, upon the first time such milestone is achieved) 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 on all products containing pegozafermin.

The FGF21 Agreement can be terminated (i) by us without cause upon 120 days' written notice to Teva, (ii) by either party, if the other party materially breaches any of its obligations under the agreement 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 glycoPEGylated FGF21 program in the event we, or any of our affiliates or sublicensees, challenges any of the Teva patents licensed to us, and the challenge is not withdrawn within 30 days of written notice from Teva.

In the fourth quarter of 2023, we made a $2.5 million milestone payment to Teva following the achievement of a clinical development milestone under the FGF21 program in SHTG. As of December 31, 2024, the timing and

likelihood of achieving any remaining milestones under the FGF21 program are uncertain. Milestone payment obligations will be recognized when payment becomes probable and reasonably estimable, which is generally upon achievement of the applicable milestone.

Bibo Collaboration Agreement

On April 4, 2024, we entered into a collaboration agreement (the "Collaboration Agreement") with BiBo Biopharma Engineering Co., Ltd., a company incorporated under the laws of the People's Republic of China ("BiBo"), pursuant to which BiBo will construct a production facility specifically designed to supply us with pegozafermin for commercialization, if approved (the "Production Facility").

Pursuant to the Collaboration Agreement, BiBo will build the Production Facility at BiBo's facility in the Lingang Special Area of China (Shanghai) Pilot Free Trade Zone to manufacture the bulk active ingredient (the "Drug Substance") required to produce pegozafermin for commercial supply. The platform is expected to provide us with manufacturing capacity to meet our commercial needs. Under the Collaboration Agreement, we are required to pay BiBo an aggregate of $135.0 million (exclusive of applicable value-added tax) toward the construction of the Production Facility (collectively, the "Payment"), of which $121.5 million (net of applicable value-added tax) in milestone payments were paid during the year ended December 31, 2024 and recorded in "Research and Development" in the consolidated statements of operations and comprehensive loss. The remaining $13.5 million will become payable upon achievement of certain specified milestones. If the actual costs of the Production Facility are substantially greater than the estimated budget, the parties will negotiate a means of allocating such cost overruns.

6. Term Loan Facility

Original Loan Agreement

In January 2023, we entered into a Loan and Security Agreement (the "Original Loan Agreement") with the lender parties thereto (the "Lenders"), K2 HealthVentures LLC as administrative agent and Ankura Trust Company, LLC as collateral agent. The Original Loan Agreement provided for a term loan facility with a maximum aggregate principal of $100.0 million, consisting of up to four separate delayed-draw term loans ("Initial Term Loan"). Upon execution of the agreement, we drew $25.0 million pursuant to the Original Loan Agreement. An additional $25.0 million expired undrawn and $50.0 million available at the Lenders' discretion lapsed upon refinancing of the debt (discussed below). Additionally, the Lenders may elect to convert up to an aggregate of $7.5 million of the principal amount of the Initial Term Loan then outstanding into shares of our common stock at a conversion price of $12.6943 per share. Notwithstanding the Loan Agreement (as defined below), this conversion right remains outstanding. The Initial Term Loan bore interest equal to the greater of (i) 8.45% and (ii) the sum of (a) the Prime Rate as reported in The Wall Street Journal plus (b) 2.25% and provided for interest-only payments through February 1, 2025. Upon prepayment or maturity, we were required to pay an end of term fee equal to 5.95% of the aggregate principal amount of term loans advanced. In connection with the Loan Agreement, the Lenders agreed to defer the payment of the existing end of term fee of $1.5 million to its originally scheduled maturity date of January 1, 2027.

In connection with the advance of the Initial Term Loan, we issued warrants to purchase 51,204 shares of our common stock, which remain outstanding as of December 31, 2024. The warrants were exercisable from the date of issuance and have a term of ten years with an exercise price of $9.76 per share. We also issued to the Lenders warrants to purchase 153,611 shares of common stock that were contingently exercisable upon funding of delayed-draw term loans. These contingently exercisable warrants were either forfeited upon expiration of the respective delayed-draw period or canceled in connection with the Loan Agreement.

Amended Loan Agreement

In September 2024, we entered into an amendment to the Original Loan Agreement (the "Amendment" and the Original Loan Agreement, as amended by the Amendment, the "Loan Agreement") increasing the maximum aggregate principal amount in delayed-draw term loans to $150.0 million (the "Term Loan") from $100.0 million. The Loan Agreement consists of (i) a first tranche of $70.0 million, of which $35.0 million was funded at closing (including the refinancing of the existing $25.0 million principal balance outstanding) and of which an additional $35.0 million is available through June 30, 2025, (ii) a second tranche of $30.0 million available to be funded upon the achievement of a specific clinical development milestone through December 31, 2025, and (iii) a third tranche of

up to $50.0 million upon our request, subject to review by the Lenders of certain information from us and discretionary approval by the Lenders.

Our obligations under the Loan Agreement are secured by substantially all of our assets, excluding intellectual property. The Loan Agreement contains customary representations and warranties, restricts certain activities and includes customary events of default, including payment default, breach of covenants, change of control, and material adverse effects. In addition, commencing January 1, 2026, we are required to maintain minimum unrestricted cash, cash equivalents and marketable securities equal to 5.0 times the average change in cash, cash equivalents and marketable securities measured over the trailing three-month period. As of December 31, 2024, we were in compliance with all covenants of the Loan Agreement.

Borrowings under the Loan Agreement mature on October 1, 2028 and provide for interest-only payments until January 1, 2027, which can be extended to January 1, 2028 upon achievement of a clinical milestone. Consecutive equal payments of principal and interest are due once the interest-only period has lapsed. The Term Loan bears interest equal to the greater of (i) 8.95% and (ii) the sum of (a) the Prime Rate as reported in The Wall Street Journal plus (b) 1.75%. On the date the debt was refinanced and on December 31, 2024, the stated interest rate on the outstanding Term Loan was 9.75% and 9.25%, respectively. An end of term fee of 5.95% of the aggregate principal amount of term loans advanced is also payable. We have the option to prepay the entire outstanding balance of borrowings under the Loan Agreement, subject to a prepayment fee ranging from 1.0% to 3.0% depending on the timing of such prepayment.

In connection with the Amendment, we issued warrants to purchase up to 406,951 shares of our common stock at an exercise price of $7.3719 per share that expire 10 years from the date of issuance. Of the 406,951 shares underlying the warrants issued, 94,955 shares were immediately exercisable upon the advance of $35.0 million at closing (including the refinancing of the existing $25.0 million principal balance outstanding) and met the criteria for equity classification. The remaining 311,996 shares become exercisable proportionally to future advances of delayed draw term loans and were liability classified and subject to remeasurement at each reporting period (see Note 3). In addition to the conversion right carried over from the Initial Term Loan, the Lenders may elect to convert up to an additional aggregate of $5.0 million of the principal amount of the Term Loan then outstanding into shares of our common stock at a conversion price of $9.5835 per share.

We evaluated the debt refinancing to determine if it was an extinguishment or a modification of the debt. Due to the addition of a substantive conversion feature (it is reasonably possible that the conversion feature may be exercised and affect the manner of the debt instrument's settlement), we determined that the refinancing was an extinguishment of debt. We measured the loss on extinguishment of debt based on the difference between the net carrying amount of the extinguished debt and the reacquisition price of the new debt, which included $0.7 million for amendment fees paid to the lender. We recorded a loss on extinguishment of debt in the amount of $1.5 million as a component of "Interest Expense" in the consolidated statements of operations and comprehensive loss for the year ended December 31, 2024.

We assessed the embedded conversion feature and concluded that bifurcation and separate accounting as a derivative liability were not required because the feature is indexed to our own stock and meets the criteria for equity classification. The immediately exercisable warrants to purchase 94,955 shares of our common stock issued to the Lenders had a fair value of $0.6 million and was recorded as debt discount with a corresponding amount to additional paid-in capital. The contingently exercisable warrants to purchase 311,996 shares of our common stock had a fair value of $0.5 million at issuance and was recorded as deferred debt issuance costs within other current assets with a corresponding entry to warrant liability (see Note 3). The deferred debt issuance costs will be amortized to interest expense over the respective delayed-draw term loan commitment periods under the Loan Agreement.

As of December 31, 2024, scheduled maturities of principal obligations under the Term Loan were as follows (in thousands):

2025	$ —
2026	—
2027	18,322
2028	16,678
Total principal outstanding	35,000
Plus accumulated accretion of end of term fees	1,306
Less unamortized debt discount	(574)
Total net carry value	35,732
Term loan, current	—
Term loan, noncurrent, net	$ 35,732

7. Stockholders' Equity

Common Stock Reserved for Issuance

Common stock reserved for future issuance, on an as-if-converted basis, were as follows:

	As of December 31,	
	2024	2023
Stock options outstanding	7,707,342	4,686,577
RSUs and PSUs outstanding	1,818,994	987,550
Shares available for future grants under equity incentive plans	2,181,235	1,790,684
Shares available for future issuance under the employee stock purchase plan	2,087,150	1,207,607
Warrants to purchase common stock outstanding	517,078	10,412,806
Pre-funded warrants to purchase common stock outstanding	4,331,081	1,881,081
Conversion feature related to outstanding term loan	1,112,546	590,816
Total shares of common stock reserved	19,755,426	21,557,121

At-the-Market ("ATM") Offerings

In March 2021, we entered into an ATM sales agreement (as amended, the "Sales Agreement") with Leerink Partners LLC and Cantor Fitzgerald & Co. (the "Sales Agents") pursuant to which we may offer and sell up to $75.0 million of shares of our common stock (the "2021 ATM Facility") from time to time pursuant to an effective registration statement. The Sales Agents are entitled to compensation at a commission of up to 3.0% of the aggregate gross sales price per share sold under the Sales Agreement. In February 2023, we entered into an amendment to the Sales Agreement, establishing a new ATM facility with an aggregate offering amount of up to $150.0 million of shares of our common stock (the "2023 ATM Facility") pursuant to an effective registration statement.

In 2022, we sold 3,948,611 shares of our common stock under the 2021 ATM Facility and received net proceeds of $28.5 million.

In 2023, we sold 2,168,539 shares of our common stock under the 2021 ATM Facility and 2023 ATM Facility and received net proceeds of $37.1 million.

In 2024, we sold 1,396,888 shares of our common stock under the 2023 ATM Facility and received net proceeds of $21.0 million. As of December 31, 2024, there was $104.4 million remaining for future sales under the 2023 ATM Facility.

Underwritten Public Offerings

In July 2022, we completed an underwritten public offering of our common stock, warrants to purchase shares of our common stock and pre-funded warrants to purchase shares of our common stock. We sold 18,675,466 shares of its common stock with accompanying warrants to purchase up to 9,337,733 shares of our common stock at a

combined public offering price of $3.55 per share. We also sold 7,944,252 pre-funded warrants to purchase shares of our common stock with accompanying warrants to purchase up to 3,972,126 shares of our common stock at a combined public offering price of $3.549 per pre-funded warrant, which represents the per share public offering price for the common stock less $0.001 per share, the exercise price for each pre-funded warrant. We raised net proceeds of $88.2 million, after deducting underwriting discounts and commissions of $5.7 million and other offering costs of $0.6 million.

The exercise of the outstanding pre-funded warrants is subject to a beneficial ownership limitation of 9.99%, or at the election of the holder prior to the issuance of the pre-funded warrant, 4.99%, which a holder may increase or decrease from time to time but shall not exceed 19.99%. The exercise price and number of shares of common stock issuable upon the exercise of pre-funded warrants are subject to adjustment in the event of any stock dividends, stock splits, reverse stock split, recapitalization, or reorganization or similar transaction, as described in the agreements. Under certain circumstances, the pre-funded warrants may be exercisable on a "cashless" basis. The common warrants and pre-funded warrants are classified as a component of stockholders' equity and additional paid-in capital because such common warrants and pre-funded warrants (i) are freestanding financial instruments that are legally detachable and separately exercisable from the equity instruments, (ii) are immediately exercisable, (iii) do not embody an obligation for us to repurchase the shares, (iv) permit the holders to receive a fixed number of common shares upon exercise, (v) are indexed to our common stock and (vi) meet the equity classification criteria. In addition, the common warrants and pre-funded warrants do not provide any guarantee of value or return.

In March 2023, we completed an underwritten public offering of our common stock. We sold 19,461,538 shares of our common stock at a public offering price of $16.25 per share. We raised aggregate proceeds of $296.8 million, net of underwriting discounts and commissions of $19.0 million and other offering costs of $0.5 million.

In December 2023, we completed an underwritten public offering of our common stock and pre-funded warrants to purchase shares of our common stock. We sold 17,567,567 shares of our common stock at a public offering price of $9.25 per share. We also sold 1,081,081 pre-funded warrants to purchase shares of our common stock at $9.249 per share, which represents the per share public offering price for the common stock less $0.001 per share, the exercise price for each pre-funded warrant. We raised net proceeds of $161.8 million, after deducting underwriting discounts and commissions of $10.4 million and other offering costs of $0.4 million. The terms and conditions of the pre-funded warrants and rights and obligations of the holder are the same as the pre-funded warrants sold in the July 2022 public offering and are described above.

In November 2024, we completed an underwritten public offering of our common stock and pre-funded warrants to purchase shares of our common stock. We sold 13,661,764 shares of our common stock at a public offering price of $8.50 per share. We also sold 3,250,000 pre-funded warrants to purchase shares of our common stock at $8.499 per share, which represents the per share public offering price for the common stock less $0.001 per share, the exercise price for each pre-funded warrant. We raised net proceeds of $136.3 million, after deducting underwriting discounts and commissions of $7.2 million and other offering costs of $0.3 million. The terms and conditions of the pre-funded warrants and rights and obligations of the holder are the same as the pre-funded warrants sold in the July 2022 public offering and are described above.

Common Stock Warrants

As of December 31, 2024, outstanding warrants to purchase shares of our common stock were as follows:

	Shares of Common Stock Underlying Warrants	Exercise Price Per Share	Expiration Date
Warrant issued in connection with term loan (SVB)	25,000	$ 22.06	June 30, 2025
Warrant issued in connection with term loan (SVB)	33,923	$ 19.12	May 28, 2031
Warrants issued in connection with term loan facility	51,204	$ 9.76	January 27, 2033
Warrants issued in connection with Term Loan facility	406,951	$ 7.372	September 30, 2034
Pre-funded warrants issued in connection with public offerings	4,331,081	$ 0.001	Do not expire
Total outstanding	4,848,159		

During the year ended December 31, 2022, pre-funded warrants to purchase 3,143,682 shares of our common stock were exercised via cashless exercises and warrants to purchase 4,202,499 shares were exercised for cash generating proceeds of $1.1 million resulting in the issuance of a total of 7,346,181 shares of common stock.

During the year ended December 31, 2023, warrants to purchase 2,927,570 shares of our common stock were exercised for cash generating proceeds of $15.6 million.

During the year ended December 31, 2024, pre-funded warrants to purchase 799,906 shares of our common stock were exercised via cashless exercises and warrants to purchase 10,179,789 shares were exercised for cash generating proceeds of $54.2 million resulting in the issuance of a total of 10,979,695 shares of common stock.

8. Stock-Based Compensation

Summary of Equity Incentive Plans

2019 Plan

In September 2019, our board of directors adopted the 2019 Equity Incentive Plan (the "2019 Plan"), which also became effective in September 2019. We 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 in an amount equal to 4% of the total number of shares of our capital stock outstanding on the immediately preceding December 31, or a lesser number of shares determined by our board of directors.

Under the 2019 Plan, we may grant incentive stock options, non-statutory stock options, stock appreciation rights, restricted stock, RSUs and other stock-based awards including PSUs. Terms of stock option agreements, including vesting requirements, are determined by our board of directors, subject to the provisions of the 2019 Plan. Stock option awards generally vest over a four-year period, with 25% of options vesting on the first anniversary of the vesting commencement date and 75% vesting ratably, on a quarterly basis, over the remaining three years. Such awards have a contractual term of ten years from the grant date. The exercise price of awards granted will not be less than the estimated fair value of the shares on the date of grant. RSUs generally vest over a two or three-year period.

Inducement Plan

In February 2023, our board of directors adopted the 2023 Inducement Plan (the "Inducement Plan") and reserved 1,500,000 shares of common stock for issuance. The Inducement Plan is a non-stockholder approved stock plan adopted pursuant to the "inducement exception" provided under Nasdaq listing rules. Under the Inducement Plan, we may grant non-statutory stock options, stock appreciation rights, restricted stock, restricted stock units and other stock-based awards to new hires who satisfy the requirements to be granted inducement grants under Nasdaq rules as an inducement material to the individual's entry into employment with us. The terms of the Inducement Plan are substantially similar to the terms of the 2019 Plan. In September 2024, the Inducement Plan was amended and restated to increase the total number of shares authorized for issuance from 1,500,000 shares to 2,500,000 shares.

Employee Stock Purchase Plan

In October 2019, our board of directors adopted the 2019 Employee Stock Purchase Plan ("ESPP"), which became effective in November 2019. We 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 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 our common stock outstanding on the immediately preceding December 31, or a lesser number of shares determined by our board of directors. We typically make two offerings each year to eligible employees to purchase stock under the ESPP with each offering having a duration of approximately six months. For each offering period, ESPP participants may purchase shares of common stock at a price per share equal to 85% of the lesser of the fair market value of our common stock on (1) the first trading day of the applicable offering period or (2) the last trading day of the applicable offering period.

Equity Incentive Plans Activity

Stock Options

The following table summarizes stock option activity for the year ended December 31, 2024:

	Number of Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term	Aggregate Intrinsic Value
			(In years)	(In thousands)
Balance outstanding as of December 31, 2023	4,686,577	$ 14.11		
Granted	3,521,200	9.42		
Exercised	(76,003)	3.19		
Canceled and forfeited	(424,432)	12.02		
Balance outstanding as of December 31, 2024	7,707,342	$ 12.19	7.9	$ 5,964
Exercisable as of December 31, 2024	3,127,295	$ 14.91	6.3	$ 5,055

The following table presents the weighted-average grant date fair value of options granted for the periods presented and the assumptions used to estimate those values using a Black-Scholes option pricing model:

	Year Ended December 31,		
	2024	2023	2022
Weighted-average grant date fair value	$7.14	$11.43	$3.38
Expected term (years)	5.5-6.1	5.5-6.1	5.5-6.3
Expected volatility	85.9-91.5%	91.5-99.2%	89.9-91.0%
Risk-free interest rate	3.5-4.6%	3.4-4.6%	1.6-3.9%
Expected dividend	—	—	—

Compensation expense related to stock option awards were $14.5 million, $11.7 million and $7.6 million for the years ended December 31, 2024, 2023 and 2022, respectively. The intrinsic value of stock options exercised during the years ended December 31, 2024, 2023 and 2022 was $0.5 million, $3.2 million and $0.6 million, respectively.

As of December 31, 2024, there was $29.1 million of unrecognized stock-based compensation related to unvested stock options, which is expected to be recognized over a weighted-average period of 2.7 years.

Restricted Stock Units and Performance Stock Units

RSUs generally vest annually over a two or three-year period. PSUs generally contain performance conditions associated with corporate goals, such as achievement of certain development milestones, that vests upon achievement over a one to three-year period.

The following table summarizes RSU and PSU activity for the year ended December 31, 2024:

	RSUs		PSUs	
	Number of Shares	Weighted-Average Grant Date Fair Value per Share	Number of Shares	Weighted-Average Grant Date Fair Value per Share
Balance outstanding as of December 31, 2023	688,382	$ 10.72	299,168	$ 5.96
Granted	1,365,850	8.88	192,000	9.98
Vested	(485,857)	9.08	(159,168)	7.00
Canceled	(64,381)	9.13	(17,000)	9.98
Balance outstanding as of December 31, 2024	1,503,994	9.65	315,000	7.67

Compensation expense related to RSUs and PSUs for the years ended December 31, 2024, 2023 and 2022 were $5.9 million, $4.3 million and $2.7 million, respectively. The total fair value of RSUs and PSUs that vested during the years ended December 31, 2024, 2023, and 2022 was $6.0 million, $7.5 million and $0.9 million, respectively.

As of December 31, 2024, total unrecognized stock-based compensation expense related to RSUs and PSUs was $12.7 million, which is expected to be recognized over a weighted-average period of 1.6 years.

ESPP

For the years ended December 31, 2024, 2023 and 2022, the number of shares of common stock issued under the ESPP were 53,151, 27,217 and 18,364, respectively.

Stock-Based Compensation Expense Allocation

The components of stock-based compensation expense recognized in the consolidated statements of operations and comprehensive loss consisted of the following (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Research and development	$ 9,279	$ 7,010	$ 4,094
General and administrative	11,355	9,096	6,262
Total stock-based compensation	$ 20,634	$ 16,106	$ 10,356

9. Income Taxes

We are subject to income taxes in the United States, including federal and state income taxes, and income taxes in Israel and Lithuania. The enacted statutory tax rates applicable to us and our significant subsidiaries were as follows:

	Year Ended December 31,		
	2024	2023	2022
89bio, Inc.	21%	21%	21%
89Bio Ltd.	23%	23%	23%
89bio Management, Inc.	21%	21%	21%
UAB 89bio Lithuania	15%	15%	15%

Components of income tax expense for the periods presented consist of the following (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Current:			
Federal	$ —	$ —	$ —
State	—	—	3
Foreign	688	3,740	16
Total current	688	3,740	19
Deferred:			
Federal	—	—	—
State	—	—	—
Foreign	4	127	—
Total deferred	4	127	—
Income tax expense	$ 692	$ 3,867	$ 19

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 our net deferred tax assets for the periods presented were as follows (in thousands):

	As of December 31,	
	2024	2023
Deferred tax assets:		
U.S. net operating loss carryforwards	$ 89,260	$ 62,873
Research and development expenses	119,428	41,834
Stock-based compensation	4,486	2,924
Accrued expenses	370	307
Operating lease liabilities	495	629
Other	1,065	378
Gross deferred tax assets	215,104	108,945
Less: valuation allowance	(214,588)	(108,230)
Total deferred tax assets	$ 516	$ 715
Deferred tax liabilities:		
Operating lease right-of-use assets	(428)	(623)
Total deferred tax liabilities	(428)	(623)
Net deferred tax assets	88	92

As of December 31, 2024 and 2023, we had valuation allowances of $214.6 million and $108.2 million, respectively, against our deferred tax assets. These valuation allowances relate to tax loss and credit 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. We regularly assess the likelihood that our deferred tax assets will be recovered from future taxable income, and to the extent we believe based upon the weight of available evidence that it is more likely than not that all or a portion of deferred tax assets will not be realized, a valuation allowance is established through an adjustment to income tax expense. The valuation allowance increased by $106.4 million in 2024 from 2023, which primarily relates to significant taxable losses.

Available Carryforward Tax Losses and Credits

As of December 31, 2024, we had an accumulated tax loss carryforward of approximately $255.5 million, $496.5 million, and $35.3 million for federal, state and Israeli tax purposes, respectively. As of December 31, 2023, we had an accumulated tax loss carryforward of approximately $195.0 million, $302.8 million, and $30.4 million for federal, state and Israeli tax purposes, respectively. 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 California will begin to expire in 2039. Carryforward tax losses in Israel have no expiration date.

As of December 31, 2024 and 2023, we had federal research and development credit carryforwards of approximately $19.7 million and $7.5 million, respectively, which expire beginning in 2040. As of December 31, 2024 and 2023, we had state research and development credit carryforwards of approximately $4.0 million and $3.2 million, respectively, which will carry forward indefinitely.

Loss from Operations, Before Income Tax

We recorded a loss from operations, before income tax for the periods presented as follows (in thousands):

	Year Ended December 31,		
	2024	2023	2022
United States	$ (366,440)	$ (138,293)	$ (101,938)
Lithuania	(59)	(59)	(7)
Israel	112	30	(62)
Net loss before income tax	$ (366,387)	$ (138,322)	$ (102,007)

Reconciliation of Income Tax Expense

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

	Year Ended December 31,		
	2024	2023	2022
Income tax benefit computed at statutory rates	$ 76,941	$ 29,054	$ 21,429
Change in valuation allowance	(106,358)	(32,248)	(33,936)
Foreign rate differential	(6)	(2)	1
State income taxes, net of federal benefit	21,924	7,653	5,824
State deferred tax true-up due to change in apportionment	(111)	2,030	6,517
Unrecognized tax benefits	(1,671)	(9,940)	—
Research and development credits, net of uncertain tax position	8,285	3,275	2,130
Executive compensation limitation	(1,930)	(3,971)	—
Other	2,234	282	(1,984)
Income tax expense	$ (692)	$ (3,867)	$ (19)

Utilization of 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

A reconciliation of the beginning and ending amount of gross unrecognized tax benefits for the years ended December 31, 2024, 2023 and 2022 is as follows (in thousands):

	As of December 31,		
	2024	2023	2022
Balance beginning of year	12,098	1,584	851
Increase (decrease) related to prior year positions	1,712	9,351	(19)
Increase related to current year positions	3,016	1,163	752
Balance end of year	16,826	12,098	1,584

Our unrecognized tax benefits, exclusive of interest, totaled $16.8 million at December 31, 2024, of which $3.6 million, if recognized, would reduce income tax expense. A material portion of our gross unrecognized tax benefits, if recognized, would increase our net operating loss carryforward and would not have an impact to the effective tax rate as it would be offset by a full valuation allowance. For the year ended December 31, 2024, the amount of gross unrecognized tax benefits related to prior year tax positions increased by $1.7 million primarily due to unresolved issues associated with tax returns for tax years 2018 through 2021 being audited by the Israel Tax Authority (“ITA”). Additionally, gross unrecognized tax benefits increased by $3.0 million related to current year tax positions, primarily due to reserves established for the federal research and development tax credit. In December 2023, we received a primary assessment from the ITA related to our 2019 reorganization and intercompany transaction to license the intellectual property rights from our Israeli subsidiary. The ITA has alleged that the transaction is deemed to be a sale of intellectual property rights. Although we believe we have adequately accounted

for our uncertain tax positions, the ultimate resolution of the ITA audit may result in payments that are materially different from what was originally recognized in our financial statements. As of December 31, 2024, discussions with the ITA are ongoing and no new information has been received that would alter our conclusions regarding the recognition and measurement of our tax positions related to this matter. We do not expect a resolution to be finalized within the next 12 months. Based on the information currently available, we do not anticipate significant increases or decreases to unrecognized tax benefits in the next twelve months. However, it is possible that such increases or decreases may occur.

We classify interest and penalties related to uncertain tax positions as income tax expense. As of December 31, 2024, the interest related to uncertain tax positions was approximately $0.6 million.

We are subject to U.S. federal income taxes, as well as income taxes in the states of California, Colorado, Indiana, Maryland, North Carolina, New Jersey, Pennsylvania, and Virginia, and in various foreign jurisdictions. To date, we have not been subject to any federal or state income tax audits. As of December 31, 2024, all tax years remain open to examination.

The Tax Cuts and Jobs Act included a change in the treatment of research and development ("R&D") expenditures for tax purposes under Section 174. Effective for tax years beginning after December 31, 2021, specified R&D expenditures must undergo a five-year amortization period for domestic spend and a 15-year amortization period for foreign spend. Prior to the effective date (2021 tax year and prior), taxpayers were able to immediately expense R&D costs under Section 174(a) or had the option to capitalize and amortize R&D expenditures over a five-year recovery period under Section 174(b). We have evaluated the current legislation at this time and prepared the provision by following the treatment of R&D expenditures for tax purposes under Section 174.

10. Net Loss Per Share

The following table presents the weighted-average shares outstanding used to calculate basic and diluted net loss per share:

	Year Ended December 31,		
	2024	2023	2022
Common stock	102,945,007	70,310,671	31,767,914
Pre-funded warrants	1,769,606	862,199	3,038,435
Total	104,714,613	71,172,870	34,806,349

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

	December 31,		
	2024	2023	2022
Stock options outstanding	7,707,342	4,686,577	3,161,917
RSUs and PSUs outstanding	1,818,994	987,550	1,095,738
Warrants to purchase common stock outstanding	517,078	10,412,806	13,166,283
Conversion feature related to outstanding term loan	1,112,546	590,816	—
Total	11,155,960	16,677,749	17,423,938

11. Segment Information

We operate and manage our business as one reportable segment, which is the business of developing and commercializing innovative therapies for the treatment of liver and cardio-metabolic diseases. Our Chief Executive Officer, as the CODM, uses consolidated net loss to evaluate our expenditures and monitor budget versus actual results. The monitoring of budgeted versus actual results and cash on hand are used in assessing performance of the segment and in establishing resource allocation across the organization.

Factors used in determining the reportable segment include the nature of our operating activities, the organizational and reporting structure and the type of information reviewed by the CODM to allocate resources and evaluate financial performance.

Significant expenses within net loss include research and development, general and administrative, interest expense, interest income and other, net and income tax expense, which are each separately presented on our consolidated statements of operations and comprehensive loss.

Our long-lived assets primarily consist of right-of-use assets related to operating leases, which are located in the United States.

12. Subsequent Events

On February 3, 2025, we completed an underwritten public offering consisting of 25,957,142 shares of common stock at an offering price of $8.75 per share, including 4,285,714 shares of common stock upon the exercise in full of the overallotment option by the underwriters, as well as pre-funded warrants to purchase 6,900,000 shares of common stock at a public offering price of $8.749 per underlying share, in each case before underwriting discounts and commissions. We raised net proceeds of approximately $269.9 million, after deducting underwriting discounts and commissions of $17.3 million and other offering costs of $0.3 million.

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, 2024, 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 our disclosure controls and procedures were effective as of December 31, 2024 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.

Changes in Internal Control over Financial Reporting

There were no changes 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, 2024 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

Our management is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rules 13a-15(f) under the Exchange Act). Internal control over financial reporting is a process designed under the supervision and with the participation of our management, including our principal executive officer and our principal financial officer, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles in the United States.

As of December 31, 2024, our management assessed the effectiveness of our internal control over financial reporting using the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in Internal Control-Integrated Framework ("2013 Framework"). Based on this assessment, our management concluded that our internal control over financial reporting was effective as of December 31, 2024.

The effectiveness of our internal control over financial reporting as of December 31, 2024 has been audited by KPMG LLP, an independent registered public accounting firm, as defined in their report which appears in Part II, Item 8 of this Annual Report on Form 10-K.

Item 9B. Other Information.

Trading Arrangements

None of our directors or executive officers adopted or terminated a Rule 10b5-1 trading arrangement or a non-Rule 10b5-1 trading arrangement during the three months ended December 31, 2024, as such terms are defined under Item 408(a) of Regulation S-K.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

The information required by this Item 10 is incorporated herein by reference to information in our proxy statement for our 2025 Annual Meeting of Stockholders (the "2025 Proxy Statement"), which we expect to be filed with the SEC within 120 days of the end of our fiscal year ended December 31, 2024, including under the heading "Information Regarding Director Nominees and Continuing Directors," "Executive Officers," "Corporate Governance," "Insider Trading Policy," and, if applicable, "Delinquent Section 16(a) Reports."

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 our website located at www.89bio.com, under "Corporate Governance." 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.

Item 11. Executive Compensation.

The information required by this Item 11 is incorporated herein by reference to information in our 2025 Proxy Statement, including under headings "Executive Compensation" and "Corporate Governance."

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

The information required by this Item 12 is incorporated herein by reference to information in our 2025 Proxy Statement, including under headings "Security Ownership of Certain Beneficial Owners and Management" and "Securities Authorized for Issuance Under Equity Compensation Plans."

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

The information required by this Item 13 is incorporated herein by reference to information in our 2025 Proxy Statement, including under headings "Director Independence" and "Certain Relationships and Related Party Transactions."

Item 14. Principal Accountant Fees and Services.

The information required by this Item 14 is incorporated herein by reference to information in our 2025 Proxy Statement, including under the heading "Ratification of Independent Auditor Appointment."

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 Current Report on Form 8-K filed on November 15, 2019)
3.2	Certificate of Amendment to the Second Amended and Restated Certificate of Incorporation of the Company (filed with the SEC as Exhibit 3.1 to the Company's Current Report on Form 8-K filed on June 9, 2023)
3.3	Third Amended and Restated Bylaws of the Company (filed with the SEC as Exhibit 3.1 to the Company's Current Report on Form 8-K filed on November 14, 2023)
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	Description of Registrant's Securities
4.3	Form of Warrant to Purchase Common Stock for Silicon Valley Bank (filed with SEC as Exhibit 4.1 to the Company's Current Report on Form 8-K filed on April 13, 2020)
4.4	Form of Warrant to Purchase Common Stock for Silicon Valley Bank (filed with the SEC as Exhibit 4.1 to the Company's Current Report on Form 8-K filed on June 4, 2021)
4.5	Form of Warrant to Purchase Common Stock for K2 HealthVentures LLC (filed with the SEC as Exhibit 4.1 to the Company's Current Report on Form 8-K/A filed on February 2, 2023)
4.6	Form of Warrant to Purchase Common Stock for K2 HealthVentures LLC (filed with the SEC as Exhibit 4.1 to the Company's Current Report on Form 8-K filed on October 3, 2024)
4.7	Form of Pre-Funded Warrant (filed with the SEC as Exhibit 4.1 to the Company's Current Report on Form 8-K filed on December 8, 2023)
4.8	Form of Pre-Funded Warrant (filed with the SEC as Exhibit 4.1 to the Company's Current Report on Form 8-K filed on November 14, 2024)
4.9	Form of Pre-Funded Warrant (filed with the SEC as Exhibit 4.1 to the Company's Current Report on Form 8-K filed on January 29, 2025)
10.1	Sales Agreement, dated March 25, 2021, by and among the Company, SVB Securities LLC and Cantor Fitzgerald & Co. (filed with the SEC as Exhibit 1.2 to the Company's Form S-3 filed on March 25, 2021)
10.2	Amendment No. 1 to Sales Agreement, dated February 15, 2023, by and among the Company, SVB Securities LLC and Cantor Fitzgerald & Co. (filed with the SEC as Exhibit 1.2 to the Company's Current Report on Form 8-K filed on February 16, 2023)
10.3+	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)
10.4+	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)
10.5+	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)
10.6+	2023 Inducement Plan (filed with the SEC as Exhibit 99.3 to the Company's Form S-8 filed on March 15, 2023)
10.7+	Amended and Restated 2023 Inducement Plan (filed with the SEC as Exhibit 10.4 to the Company's Form 10-Q filed on November 7, 2024)

Exhibit Number	Description
10.8+	Executive Employment Offer Letter, dated April 15, 2020, by and between the Company and Rohan Palekar (filed with the SEC as Exhibit 10.1 to the Company's Current Report on Form 8-K filed on May 4, 2020)
10.9+	Executive Employment Offer Letter, dated April 15, 2020, by and between the Company and Hank Mansbach (filed with the SEC as Exhibit 10.3 to the Company's Current Report on Form 8-K filed on May 4, 2020)
10.10+	Executive Employment Offer Letter, dated April 15, 2020, by and between the Company and Quoc Le-Nguyen (filed with the SEC as Exhibit 10.4 to the Company's Current Report on Form 8-K filed on May 4, 2020)
10.11+	Executive Employment Offer Letter, dated April 15, 2020, by and between the Company and Ryan Martins (filed with the SEC as Exhibit 10.2 to the Company's Current Report on Form 8-K filed on May 4, 2020)
10.12+	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)
10.13+	Executive Employment Offer Letter, dated July 31, 2024, by and between the Company and Francis Sarena (filed with the SEC as Exhibit 10.1 to the Company's Form 10-Q filed on November 7, 2024)
10.14†	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)
10.15†	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)
10.16†	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)
10.17†	Master Contract Services Agreement by and between the Company and BiBo Biopharma Engineering Co., Ltd., dated as of February 10, 2023, as amended (filed with the SEC as Exhibit 10.4 to the Company's Quarterly Report on Form 10-Q filed on May 8, 2023)
10.18	Office Sublease by and between 89bio, Inc. and Sender, Inc., dated as of October 20, 2023 (filed with the SEC as Exhibit 10.2 to the Company's Form 10-Q filed on November 7, 2024)
10.19	Loan and Security Agreement, dated as of January 4, 2023, among the Company, 89bio Management, Inc., 89Bio Ltd., K2 HealthVentures LLC and Ankura Trust Company, LLC (filed with the SEC as Exhibit 10.1 to the Company's Current Report on Form 8-K filed January 6, 2023)
10.20	Amendment to Loan and Security Agreement, dated as of September 30, 2024, among the Company, 89bio Management, Inc., 89Bio Ltd., K2 HealthVentures LLC and Ankura Trust Company, LLC (filed with the SEC as Exhibit 10.3 to the Company's Form 10-Q filed on November 7, 2024)
10.21	Collaboration Agreement, dated as of April 4, 2024, by and between the Company and BiBo Biopharma Engineering Co., Ltd. (filed with the SEC as Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q filed August 5, 2024)
10.22*	Insider Trading Policy
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
24.1*	Power of Attorney
31.1*	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934

Exhibit Number	Description
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
97.1	Incentive Compensation Clawback Policy (filed with the SEC as Exhibit 97.1 to the Company's Form 10-K filed on March 1, 2024)
101.INS	Inline XBRL Instance Document
101.SCH	Inline XBRL Taxonomy Extension Schema With Embedded Linkbase Documents
104	Cover Page Interactive Data File

* 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: February 27, 2025

By: /s/ Rohan Palekar

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

Date: February 27, 2025

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, 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*)	February 27, 2025
/s/ Ryan Martins **Ryan Martins**	Chief Financial Officer (*principal financial and accounting officer*)	February 27, 2025
/s/ Steven Altschuler **Steven Altschuler, M.D.**	Director	February 27, 2025
/s/ Edward Morrow Atkinson III **Edward Morrow Atkinson III**	Director	February 27, 2025
/s/ Martin Babler **Martin Babler**	Director	February 27, 2025
/s/ Derek DiRocco **Derek DiRocco, Ph.D.**	Director	February 27, 2025
/s/ Michael Hayden **Michael Hayden, M.B., Ch.B., Ph.D.**	Director	February 27, 2025
/s/ Kathleen D. LaPorte **Kathleen D. LaPorte**	Director	February 27, 2025
/s/ Charles McWherter **Charles McWherter, Ph.D.**	Director	February 27, 2025
/s/ Lota Zoth **Lota Zoth, C.P.A.**	Director	February 27, 2025

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