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, 2020

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 001-36287

Flexion Therapeutics, Inc.

(Exact name of Registrant as specified in its Charter)

Delaware	**26-1388364**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
10 Mall Road, Suite 301 Burlington, Massachusetts	**01803**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (781) 305-7777

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, $0.001 par value per share	FLXN	The 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, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

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

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

Indicate by check mark whether the registrant 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 ☒

The aggregate market value of the Registrant's voting and non-voting common equity held by non-affiliates of the Registrant, based on the closing price of the shares of common stock on The Nasdaq Stock Market on June 30, 2020, was $587,558,188.

The number of shares of the Registrant's common stock outstanding as of March 1, 2021, was 49,924,004.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's proxy statement to be filed with the Securities and Exchange Commission pursuant to Regulation 14A in connection with the Registrant's 2021 Annual Meeting of Stockholders, which will be filed subsequent to the date hereof, are incorporated by reference into Part III of this Form 10-K. Such proxy statement will be filed with the Securities and Exchange Commission not later than 120 days following the end of the Registrant's fiscal year ended December 31, 2020.

FLEXION THERAPEUTICS, INC.
FORM 10-K—ANNUAL REPORT
For the Fiscal Year Ended December 31, 2020

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PART I

Special Note Regarding Forward-Looking Statements

This Annual Report on Form 10-K, or this Annual Report, contains "forward-looking statements"— that is, statements related to future, not past, events— as defined in Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, that reflect our current expectations regarding our future discovery, development and commercialization activities, results of operations, financial condition, cash flows, performance and business prospects, and opportunities, as well as assumptions made by, and information currently available to, our management. Forward-looking statements include any statement that does not directly relate to a current or historical fact. We have tried to identify forward-looking statements by using words such as "believe," "may," "could," "will," "estimate," "continue," "anticipate," "intend," "seek," "plan," "expect," "should," or "would." Among the factors that could cause actual results to differ materially from those indicated in the forward-looking statements are risks and uncertainties inherent in our business including, without limitation: we have incurred significant losses since our inception and we expect to incur substantial losses for the foreseeable future and may never achieve or maintain profitability; we have a limited history of commercializing ZILRETTA® and have not received regulatory approval for any other product candidates; we may require additional capital prior to completing development and commercializing any of our product candidates in development; we may be unable to successfully commercialize ZILRETTA or any of our other product candidates; risks related to clinical development, including the fact that the results of on-going or future clinical trials may not be consistent with past results; we rely on third parties to manufacture and conduct the clinical trials of ZILRETTA and our development-stage product candidates, which could limit our commercialization efforts or delay or limit their future development or regulatory approval; we may be unable to adequately maintain and protect our proprietary intellectual property assets, which could impair our commercial opportunities; and other risks detailed below in "Item 1A. Risk Factors."

Although we believe that the expectations reflected in our forward-looking statements are reasonable, we cannot guarantee future results, events, levels of activity, performance or achievement. We undertake no obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events or otherwise, unless required by law.

Item 1. Business

Unless the content requires otherwise, references to “Flexion,” “Company,” “we,” “our,” and “us” in this Annual Report refer to Flexion Therapeutics, Inc. and our subsidiary, Flexion Therapeutics Securities Corporation.

Overview

We are a biopharmaceutical company focused on the discovery, development and commercialization of novel, local therapies for the treatment of patients with musculoskeletal conditions, beginning with osteoarthritis, or OA, the most common form of arthritis. We have an approved product, ZILRETTA®, which we market in the United States. ZILRETTA is the first and only extended-release, intra-articular, or IA (meaning in the joint), injection indicated for the management of OA knee pain. ZILRETTA is a non-opioid therapy that employs our proprietary microsphere technology to provide effective pain relief. The pivotal Phase 3 trial, on which the approval of ZILRETTA was based, showed that ZILRETTA met the primary endpoint of pain reduction at Week 12, with statistically significant pain relief extending through Week 16.

ZILRETTA was approved by the U.S. Food & Drug Administration, or FDA, on October 6, 2017, and launched in the United States shortly thereafter. We market ZILRETTA to prescribing physicians through our own field sales force of approximately 100 Musculoskeletal Business Managers, or MBMs.

ZILRETTA combines a commonly administered steroid, triamcinolone acetonide, or TA, with poly lactic-co-glycolic acid, referred to as PLGA, delivering a 32 mg dose of TA to provide extended therapeutic concentrations in the joint and persistent analgesic effect. Both the magnitude and duration of pain relief provided by ZILRETTA in clinical trials were clinically meaningful with the magnitude of pain relief amongst the largest seen to date in OA clinical trials. The overall frequency of treatment-related adverse events in these trials was similar to those observed with placebo, and no drug-related serious adverse events were reported.

Based on the strength of our pivotal and other clinical trials, we believe that ZILRETTA represents an important treatment option for the millions of patients in the U.S. who are in need of safe and effective extended relief from OA knee pain. ZILRETTA is uniquely distinguished by the following attributes:

- in the Phase 3 trial,
  - statistically significant pain relief against placebo (saline) as measured by the weekly mean of the Average Daily Pain, or ADP, score:
    - demonstrated at week 12, the primary endpoint, a p-value of <0.0001, 2-sided, with benefits extending through week 16; and
    - at each week beginning at week 1 and continuing through week 12 nearly 60% of patients reported no pain or mild pain;
  - statistically significant change from baseline as compared to placebo in weekly ADP intensity score through week 12 as measured by the area under effect curve ($p<0.0001$) (demonstrating a 50% reduction from baseline);
  - numeric improvement when compared with placebo and immediate-release TA at each time point through 12 weeks on exploratory measures – WOMAC A (pain), WOMAC B (stiffness) and WOMAC C (function) and the Knee Injury and Osteoarthritis Outcome Score (KOOS) quality of life subscale; and
  - reduced rescue medicine consumption compared with placebo and immediate-release TA (exploratory endpoint);
- an acceptable safety profile with side effects similar to placebo;
- statistically significant ($p<0.05$, 2-sided) reduction in the rise of blood glucose compared to that observed following immediate-release TA injection in patients with Type 2 diabetes who also have knee OA as measured by change in average blood glucose from baseline to 72 hours post injection; and
- persistent concentrations of drug in the joint.

ZILRETTA has demonstrated significant, durable relief of OA knee pain and, as such, can address an important unmet need among patients, physicians and healthcare payers. We believe that ZILRETTA holds the potential to become a leading IA medicine for OA knee pain.

We believe ZILRETTA’s extended-release profile may also provide effective treatment for OA pain of the shoulder, and we intend to initiate a trial investigating ZILRETTA in shoulder OA in 2021.

OA is a type of degenerative arthritis that is caused by the progressive breakdown and eventual loss of cartilage in one or more joints. Arthritis is the most common cause of disability in the U.S. and OA is the most common joint disease, affecting more than 32.5 million adults in the U.S. and these numbers are expected to grow as a result of aging, obesity and sports

injuries. OA commonly affects large weight-bearing joints like the knees and hips, but also occurs in the shoulders, hands, feet and spine. Patients with OA suffer from joint pain, tenderness, stiffness and limited movement. As the disease progresses, it becomes increasingly painful and debilitating, culminating, in many cases, in the need for total joint arthroplasty, or TJA.

Because there is no cure for OA, controlling pain, maintaining function, and delaying surgery are the primary goals of prescribing clinicians. Oral drugs, such as non-steroidal anti-inflammatory drugs, or NSAIDs, including COX II inhibitors, and serotonin and norepinephrine reuptake inhibitors, or SNRIs, as well as topical NSAIDs, are used to treat early-stage OA pain but have limited effect and, given the amount and frequency of use in OA patients, are associated with serious side effects. For example, NSAIDs have shown increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke. Furthermore, this class of drugs can cause serious gastrointestinal adverse events including bleeding, ulceration and perforation of the stomach or intestines. These serious side effects are particularly worrisome because OA patients often have co-existing medical conditions, including diabetes and hypertension. For patients with moderate to severe OA pain, IA medicines, such as immediate-release steroids and hyaluronic acid, or HA, injected into the joint, are generally considered well-tolerated, but they leave the joint rapidly and often fail to produce or maintain clinically meaningful pain relief. Physicians may prescribe opioids, which in addition to the serious risk of addiction and abuse, have numerous serious side effects including respiratory depression, hypotension, constipation, cardiac events, and deaths from unintentional overdose. As a result of these limitations, many OA patients experience persistent and worsening pain, which often culminates in the decision to have TJA, a painful and expensive procedure. Further, because the initial joint replacement wears out over time, the younger the patient is at the time of the joint replacement, the more likely it is that he or she will require repeat surgery in their lifetime.

According to IQVIA, in 2019 approximately 5 million patients in the U.S. received an IA injection treatment for knee OA pain. That population was comprised of approximately 4.2 million patients who were treated with immediate-release steroids and roughly 1 million patients who received hyaluronic acid, or HA, with some patients receiving both treatments in the same year. The HA utilization occurred despite guidance from prominent medical societies, including the American Academy of Orthopedic Surgeons stating that HA is an ineffective treatment for knee OA, and a number of major commercial payers no longer reimburse for the entire class of HA products. In addition, according to SmartTRAK in 2019, HA sales in the U.S. were $1 billion, with a cost per course of treatment ranging from $245 to $2,000. Our commercial experience indicates that, given the limitations of immediate-release steroids and HAs, physicians are open to new treatment options, like ZILRETTA, which can provide their patients with enhanced durable pain relief.

Additionally, IQVIA data indicate that, in 2019, healthcare practitioners administered roughly 600,000 immediate release steroid injections for the treatment of shoulder OA. We intend to initiate a trial investigating ZILRETTA in shoulder OA in 2021.

We have a growing pipeline with two product candidates focused on the local treatment of musculoskeletal conditions: FX201 and FX301. FX201 is a gene therapy product candidate designed to provide “on demand” production of an anti-inflammatory protein, interleukin-1 receptor antagonist (IL-1Ra) whenever inflammation is detected in the joint. We believe FX201 has the potential to provide at least six months to one year of pain relief from OA of the knee and improve function. Presently, there are no approved disease modifying treatments for OA; however, based on its mechanism of action, we believe FX201 also holds the potential to modify disease progression. In October of 2019, the FDA cleared the Investigational New Drug (IND) application for FX201, allowing for initiation of a Phase 1 open-label dose-escalation study to test three doses (low, mid, and high) of FX201 in cohorts of five to eight patients. In February 2021, we announced plans to advance to the high dose cohort and expand the low and mid dose treatment cohorts to include up to an additional 20 patients in each group.

FX301, is a locally administered NaV1.7 inhibitor, known as funapide, formulated for extended release in a thermosensitive hydrogel. The initial development of FX301 is intended to support administration as a peripheral analgesic nerve block for management of post-operative pain. We believe FX301 has the potential to provide effective, non-opioid pain relief for at least 3-5 days, while preserving extremity motor function, which is typically compromised by local anesthetic peripheral nerve block. In February 2021, FDA cleared the IND application for FX301. We plan to initiate a Phase 1b proof of concept clinical trial of FX301 administered as a popliteal fossa block (a commonly used nerve block in foot and ankle-related surgeries) in patients undergoing bunionectomy and expect to treat the first patient in the first half of this year.

We have worldwide commercialization rights for ZILRETTA, FX201 and FX301. We also have an exclusive worldwide license agreement with Southwest Research Institute, or SwRI®, with respect to the use of SwRI’s proprietary microsphere manufacturing technologies for certain steroids formulated with PLGA, including ZILRETTA. Our PLGA formulation technology is protected through a combination of patents, trade secrets, and proprietary know-how. In addition, we own or have rights to various trademarks, copyrights and trade names used in our business, including FLEXION®, ZILRETTA® and FLEXFORWARD®. Our logos and trademarks are the property of Flexion Therapeutics, Inc. All other brand names or trademarks appearing in this report are the property of their respective holders. Use or display by us of other parties’

trademarks, trade dress, or products in this report is not intended to, and does not, imply a relationship with, or endorsement or sponsorship of us, by the trademark or trade dress owners.

Our Strategy

Our goal is to cost-effectively discover, develop and commercialize novel, locally administered medicines that can safely and effectively address significant unmet medical needs associated with musculoskeletal conditions, with a particular interest in OA, post-operative pain and low back pain. The principal elements of our strategy include the following:

- ***Establish ZILRETTA as the leading IA treatment for OA knee pain and maximize its value by expanding approved indications.*** Based on ZILRETTA's clinical profile, we believe that it can be the first-line IA therapy for OA knee pain. Immediate-release IA steroids leave the joint rapidly and typically fail to confer adequate pain relief beyond 6-8 weeks. Since, by medical practice, steroids typically are not injected more frequently than every three months, patients often experience inadequate magnitude or duration of pain relief during that time. ZILRETTA is specifically formulated using our proprietary PLGA-based microsphere technology to slowly and continuously release drug in the joint for over 12 weeks. Our clinical data support the ability of ZILRETTA to provide substantial magnitude and durability of OA knee pain relief following administration.

  ZILRETTA is currently approved for the treatment of OA knee pain, but we believe that it has the potential for broader use in patients with OA, specifically in the shoulder. We intend to initiate a trial investigating ZILRETTA in shoulder OA in 2021.
- ***Bolster our robust pipeline of high-quality product candidates to address unmet medical needs.*** We seek to advance our product candidates, FX201 and FX301, and further build our product pipeline through a combination of internal research and selective business development activities. Our Flexion Innovation Lab in Woburn, Massachusetts has been integral in supporting our research and development activities.
- ***Leverage our infrastructure to efficiently and cost-effectively develop and commercialize ZILRETTA and our product candidates***. We have built up extensive knowledge, expertise and capabilities in the development and commercialization of locally delivered medicines for musculoskeletal conditions.
- ***Retain commercial rights in the United States and selectively partner outside of the United States.*** Because IA therapies in the United States are administered by a relatively small number of specialists, particularly orthopedists, non-operative sports medicine physicians, and rheumatologists, we believe we can realize the greatest value for our shareholders by fully leveraging our know-how, capabilities and infrastructure. The U.S. represents the most attractive market for ZILRETTA, and potentially for FX201 and FX301, and as a result, we aim to retain the commercial rights to our product and programs in the U.S. while we look to selectively engage partners outside of the United States.

COVID-19

On March 11, 2020, the World Health Organization made the assessment that a novel strain of coronavirus, which causes the COVID-19 disease, had become a global pandemic ("COVID-19"). COVID-19 has presented a substantial public health and economic challenge around the world. In mid-March of 2020, the U.S. declared a national emergency and states implemented various "social distancing" and "stay at home" measures to mitigate the spread of COVID-19. In turn, we closed our offices in Burlington, MA, and instructed all of our employees to work from home, including all of our field-based personnel. We also undertook prudent and disciplined steps to reduce expenses across the organization, including hiring and travel freezes, elimination of our in-person presence at medical and industry conferences, reductions in in-person physician speaker programs, reductions in select marketing programs and materials, and elimination of non-essential operating expenses. In addition, we paused our Phase 1 trial of FX201 and discontinued our Phase 2 trial investigating ZILRETTA in shoulder OA and adhesive capsulitis (AC) due to the small number of patients enrolled in the trial, the uncertainty around when we would be able to restart the study, as well as the costs required to maintain it in an inactive status. We also temporarily paused manufacturing activities for ZILRETTA to avoid excess levels of inventory. Refer to Management's Discussion and Analysis of Financial Condition and Results of Operations (Part II, Item 7 of this Annual Report) for further discussion regarding the impact of COVID-19 on our fiscal year 2020 financial results.

The COVID-19 pandemic has caused significant volatility and uncertainty that has disrupted and is expected to continue to disrupt our business. Any prolonged material future disruptions to the work of our employees, suppliers, contract manufacturers, or vendors, or to the operations of physicians that administer ZILRETTA could negatively impact our operations, availability of supplies, carrying value of assets, operating results or cash flows. The extent to which the COVID-19 pandemic impacts our business going forward will depend on numerous evolving factors we cannot reliably predict, including the duration and scope of the pandemic; governmental, business, and individuals' actions in response to the pandemic; access to, utilization of, and efficacy of COVID-19 vaccines; and the impact on economic activity including the

possibility of recession or financial market instability. Refer to Risk Factors (Part I, Item 1A of this Annual Report) for a discussion of these factors and other risks.

Osteoarthritis

OA, also referred to as degenerative joint disease, is the most common form of arthritis in the U.S. according to the U.S. Centers for Disease Control and Prevention, or the CDC, affecting more than 32.5 million adults, and its prevalence is expected to grow in the years ahead . Furthermore, while often perceived as "just a routine part of aging," OA is a serious disease that is associated with significant costs to healthcare systems and increased risk of mortality:

- According to the CDC, approximately 40% of U.S. adults are obese, which increases the risk of developing OA.
- Knee injury is common, particularly amongst young athletes, and increases the risk of developing OA later in life by more than five-fold.
- In 2013, the total national arthritis-attributable medical care costs and earnings losses among adults with arthritis were $303.5 billion.
- According to a study published by the Osteoarthritis Research Society International ("OARSI"), U.S. patients with symptomatic radiographic knee OA were 23% more likely to die prematurely than people free from OA independent of age, sex, and race.

The CDC estimates that one of every two people in the U.S. is expected to develop symptomatic knee OA, the most common form of OA during their lifetime and of those who develop symptomatic knee OA, one in two will progress to total knee replacement. Recent research indicates that the average age of physician-diagnosed knee OA has fallen by 16 years, from age 72 in the 1990s to age 56 in the 2010s. According to the same research, U.S. adults between the ages of 35 and 84 in the early 2010s will account for approximately 6.5 million new cases of knee OA over the next decade.

Common Treatments for OA

OA is a progressive disease for which there is no cure. As a result, current treatments are intended to address the symptoms of the disease, in particular, relief of pain and improvement in functional status.

In early-stage disease, treatment begins with non-pharmacologic therapy including exercise, weight control and physical therapy. As the disease progresses, physicians prescribe pharmacologic therapy, typically beginning with acetaminophen and progressing to oral NSAIDs, including COX II inhibitors, topical NSAIDs or SNRIs. Physicians may also treat OA pain with opioids; however, these drugs have serious drawbacks and are generally considered to be a suboptimal therapy for chronic non-cancer pain, like that associated with OA.

When non-pharmacologic therapy, oral, and topical pain medications prove inadequate, physicians typically transition patients to IA injections. Immediate-release steroids have historically served as the first line IA therapy, and TA, the corticosteroid used in ZILRETTA, is amongst the most commonly prescribed IA corticosteroid injections. When immediate-release steroids no longer provide sufficiently durable pain relief, patients may progress to IA HA, a significantly more expensive therapy with only marginally greater effect than placebo.

Due to severe pain that can no longer be controlled therapeutically, many patients opt to have TJA, which is costly and painful. One of the most prevalent TJA procedures in the U.S. is total knee arthroplasty. Compared to existing drug therapy, total knee arthroplasty is very expensive, with average costs ranging between $25,000 and $60,000, and many patients (approximately 20%) are dissatisfied with the outcome of this procedure. The earlier a patient undergoes TJA, the more likely it is that the knee implant will wear out over time and they will require revision surgery in following years. According to IQVIA, in 2019, there were approximately 1.4 million total knee arthroplasties performed in the U.S.

Limitations of Common Treatments for OA

Oral therapies, such as NSAIDs, may offer adequate analgesia for early-stage OA pain, but they may be associated with serious side effects such as gastrointestinal bleeding, cardiovascular events and other adverse events. For example, SNRIs may have a role in worsening depression and the emergence of suicidality in certain patients. In addition to their serious side effects, oral drugs may provide limited pain relief and eventually can become insufficient to control OA pain for many patients as the disease progresses.

IA therapies, including immediate-release steroids, and HAs, are generally well-tolerated but provide pain relief that is often insufficient or inadequate in duration. Immediate-release suspensions or solutions typically leave the joint within hours to days, and they are rapidly absorbed systemically, which may result in undesirable side effects. For example, IA immediate-release steroid injections are associated with a rapid elevation of blood glucose in diabetics, which can be of clinical concern. While IA steroids demonstrate large initial analgesic effects relative to other therapies, as a result of leaving the joint quickly, IA steroids typically fail to confer adequate pain relief beyond 6-8 weeks. In addition, current clinical practice generally

indicates that IA steroid suspensions not be administered more frequently than once every three months. Based on our market research, approximately 50% of patients surveyed who received IA immediate-release steroids were unsatisfied with the duration of benefit.

Despite estimated U.S. sales of approximately $1 billion in 2019, IA HAs, which are approved only for use in the knee, produce only marginally more effective pain relief than placebo and may have no discernible effect on a patient's ability to carry out their daily activities.

While the consequences from the overuse and abuse of opioids are well-known, these powerful medicines are still commonly prescribed for OA related pain, despite the fact that they are not an effective treatment for this chronic condition. A recent study estimated that as many as 70% of patients who are prescribed a medicine for OA pain will receive an opioid because physicians have so few effective treatment options. We further believe that the growing societal awareness of the risks posed by opioids may make new treatment options attractive for patients and physicians seeking non-opioid alternatives. Beyond the significant concerns related to the potential for overuse and abuse, opioid use is also associated with unintentional overdose which can produce respiratory depression, hypotension, cardiac events and death.

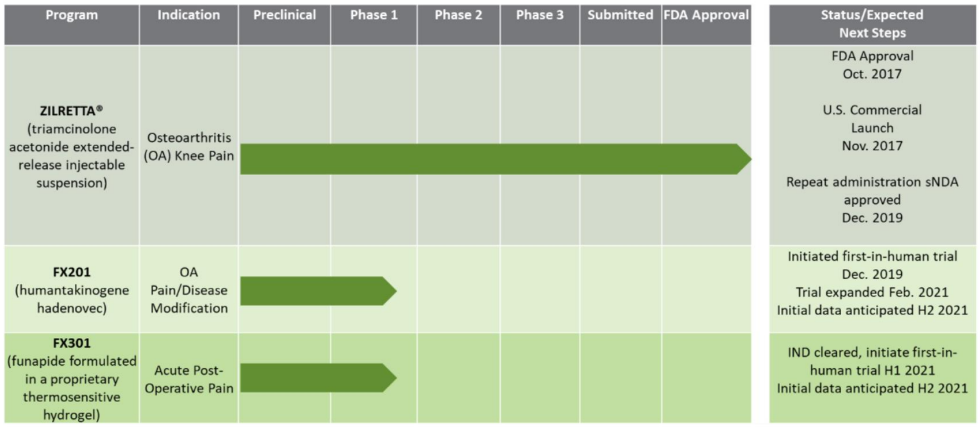
The Flexion Extended-Release Microsphere Technology

Our extended-release technology allows us to incorporate active pharmaceutical ingredients in PLGA microspheres. We believe we are the first company to administer PLGA microspheres into a human joint. PLGA is a proven extended-release delivery vehicle that is metabolized to carbon dioxide and water as it releases drug in the IA space and is used in other approved drug products and surgical devices. The technology is designed to enable novel formulations of pharmaceuticals by providing extended-release of drugs over time and the physical properties of the polymer-drug matrix can be varied to achieve specified drug loads and release rates. Key to the success of our IA therapies is the ability to maintain persistent concentrations of drug in the joint, while minimizing systemic exposure. Utilizing our PLGA microsphere technology, ZILRETTA is the first and only approved extended-release, IA therapy for patients confronting OA-related knee pain.

We believe ZILRETTA and our technology will be protected primarily through a combination of patents, trade secrets and proprietary know-how, and we intend to seek marketing exclusivity for any approved products. A composition of matter patent has been issued by the United States Patent and Trademark Office, or U.S. PTO, for ZILRETTA, with a patent term into 2031. The U.S. PTO has also issued two patents directed at the methods of manufacturing and using ZILRETTA with patent terms into 2031. Considerable expertise and effort were required to carry out the large body of original work underlying the formulation of ZILRETTA, including experimenting with, and observing the effects of over 50 steroid and PLGA formulations. We believe our extensive know-how and trade secrets relating to the manufacturing process for ZILRETTA, including those that relate to precise pharmaceutical release profiles, represent a meaningful entry barrier.

Approved Product and Pipeline Programs

Our pipeline strategy is to continue to study ZILRETTA in other areas and, if feasible, expand ZILRETTA's product label to include additional indications and broaden its scope of administration, advance our other product candidates, FX201 and FX301, through clinical development and build a robust pipeline of additional locally administered therapies to address musculoskeletal conditions.



ZILRETTA – FDA Approved Product for the Management of OA Knee Pain

Key Regulatory Developments

On October 6, 2017, ZILRETTA received approval from the FDA for the management of OA pain of the knee. ZILRETTA is the first and only approved extended-release, IA therapy for OA knee pain. It is a non-opioid medicine that employs our proprietary microsphere technology to provide proven pain relief. The approval was based upon data from the pivotal Phase 3 clinical trial, a randomized, double-blind study which evaluated 484 patients at 37 centers worldwide. The pivotal Phase 3 trial showed that ZILRETTA met the primary endpoint of pain reduction at Week 12, with statistically significant pain relief extending through Week 16. ZILRETTA's label reflects its strong safety profile and states the most commonly reported adverse reactions (incidence ≥1%) in clinical studies included sinusitis, cough and contusions.

In December 2018, we submitted a supplemental new drug application, or sNDA, to the FDA to revise the product label for ZILRETTA to allow for repeat administration. The sNDA submission was based on data from a Phase 3b single-arm, open-label clinical trial.

On December 26, 2019, we announced that the FDA approved the sNDA. The revised product label removed language which previously stated that ZILRETTA was "not intended for repeat administration" and replaced it with language stating that "the efficacy and safety of repeat administration of ZILRETTA have not been demonstrated." The new label also includes a study description and safety data from the Phase 3b repeat administration trial and nonclinical toxicology data from previously submitted single and repeat administration studies in non-diseased animals.

Summary of Active, Planned and Key Completed Clinical Trials

Prior to FDA approval, we completed seven clinical trials evaluating ZILRETTA (also known as FX006) against either immediate release TA crystalline suspension, or TAcs, placebo (saline), or both in patients with OA of the knee. In total, 424 patients were treated with a single IA injection (32mg) of ZILRETTA in those trials. We believe ZILRETTA's extended-release profile may also provide effective treatment for OA pain of the shoulder, and we intend to initiate a trial investigating ZILRETTA in shoulder OA in 2021.

Manufacturing

We believe that the multifaceted nature of PLGA drug product manufacturing and the limited number of capable contract manufacturing companies that offer PLGA drug product manufacturing creates an entry barrier. The technology is designed to enable novel formulations of pharmaceuticals by providing extended-release of drugs over time and the physical properties of the polymer-drug matrix can be varied to achieve specified drug loads and release rates.

We utilize contract manufacturers to produce the drug substances and drug products used in ZILRETTA. Manufacture of PLGA microspheres is a complex process and there are a limited number of contract manufacturing sites with PLGA experience. Our proprietary injectable IA extended-release technology allows us to incorporate pharmaceuticals in PLGA microspheres, such as TA, in the case of ZILRETTA, as well as potentially other product candidates. Following extensive

development programs, we have established that a single injection of ZILRETTA sustains local concentrations of TA in the joint for several months. The ZILRETTA microsphere PLGA formulation has gone through numerous iterations and has been optimized to release the drug over an extended period of time. In developing this unique combination of manufacturing process and formulation, we have established numerous trade secrets that relate to precise pharmaceutical release profiles.

The active pharmaceutical ingredient in ZILRETTA, TA, is manufactured and supplied by Farmabios SpA in accordance with current Good Manufacturing Practice, or cGMP, standards. This supplier is subject to regular inspections by the FDA. The PLGA material used in the manufacture of ZILRETTA is supplied by Evonik Corporation, or Evonik. In November 2016, we entered into a Supply Agreement with Evonik for the purchase of PLGA for clinical and commercial supply of ZILRETTA. The initial term of the Supply Agreement is until July 2021 and will renew for two successive two-year terms upon mutual written consent by both parties. Under the Supply Agreement, we are bound to purchase PLGA from Evonik at certain minimum purchase amounts, which decrease over time, and at a specified price per gram, subject to adjustment from time to time, including due to changes in price indices and in the event the initial term of the Supply Agreement is extended. Upon termination of the Supply Agreement (other than termination due to the bankruptcy of either Evonik or us) we are obligated to pay the costs associated with the binding supply forecast provided to Evonik.

In August 2015, we entered into a Manufacturing Agreement with Patheon U.K. Limited, or Patheon, for the manufacture of clinical and commercial supplies of ZILRETTA finished drug product. In connection with the agreement, Patheon undertook certain technical transfer activities and construction services to prepare its United Kingdom facility for the manufacture of ZILRETTA in dedicated manufacturing suites. The initial term of our Manufacturing Agreement with Patheon is until October 2027. We may terminate this agreement upon one month's notice if a regulatory authority causes the withdrawal from, or halts development of, ZILRETTA (in either case for reasons outside our reasonable control) in the United States or any other market that represents 80% of our overall sales. We may also terminate this agreement at any time for convenience by providing 24 months' notice. Either we or Patheon may terminate this Agreement in the event of (a) an unremedied material breach or bankruptcy of the other party, (b) if a material force majeure event remains uncured for a period of more than 90 days and (c) the granting of a permanent injunction to a third party claiming intellectual property infringement of ZILRETTA in the United States or UK. Upon termination of this agreement, we are obligated to pay for the costs associated with the removal of our manufacturing equipment and for Patheon's termination costs up to a specified maximum amount.

In July 2014, we executed an exclusive worldwide licensing agreement with Southwest Research Institute Manufacturing®, or SwRI, to utilize proprietary microsphere manufacturing technologies for production of our extended-release drug candidates, including ZILRETTA. The SwRI technologies employ a uniquely controlled and continuous atomizing technology that facilitated scale-up of commercial supply. This exclusive agreement provides for an expanded field of use in a variety of musculoskeletal disorders, as well as broader polymer and steroid ranges, which offers the flexibility to potentially explore different doses, disease indications, and drug-PLGA combinations. We have no further payment obligations following the amendment executed by the parties in February 2017 and the license remains in effect through patent term expiry.

Commercial Strategy

We have established a commercial infrastructure, including approximately 100 MBMs, intended to drive the adoption of ZILRETTA among the approximately 11,000 prescribers who treat approximately 70% of patients diagnosed with OA pain of the knee who receive an IA treatment. Of these prescribers, approximately 75% reside within orthopedic practices (including orthopedists, physician assistants, and nurse practitioners) with the balance comprised of a mix of rheumatologists, sports medicine physicians, and pain specialists. We distribute ZILRETTA through a limited network of third-party specialty distributors, a specialty pharmacy, group purchasing organizations, and other third parties. While we believe that the United States represents the most attractive market for ZILRETTA, we continue to evaluate opportunities and potential partnerships to develop and commercialize ZILRETTA in territories outside the United States where we believe there is the potential for value-based pricing and reimbursement.

Flexion currently targets over 5,000 customer accounts, predominantly made up of orthopedic practices, with the goal of moving them through the ZILRETTA utilization continuum from trial to adoption as a standardized part of the treatment continuum across the field of patients with OA pain of the knee. The sales force effort is supported by a number of programs that include peer-to-peer engagement, direct-to-patient initiatives, and media campaigns designed to raise awareness of knee OA and the impact that ZILRETTA can have in effectively managing patients who suffer from it.

FX201

FX201 is an IA gene therapy candidate which is designed to induce the local production of interleukin-1 receptor antagonist (IL-1Ra), an anti-inflammatory protein. Preclinical data suggest that following injection of FX201, its genetic material is incorporated into local cells, and IL-1Ra is expressed in response to inflammation in the joint tissues. Inflammation is a known cause of pain, and chronic inflammation is thought to play a major role in the progression of OA. By persistently suppressing inflammation, we believe FX201 has the potential to both reduce pain and possibly modify disease progression.

In early October 2019, the FDA cleared the IND application for FX201, and we subsequently initiated a Phase 1 first-in-human trial. Nonclinical safety and efficacy data submitted in the IND application indicated that a single administration of FX201 was well-tolerated, had no significant biodistribution outside the target tissues, and pharmacology studies with the rat, mouse, and horse orthologues in animal models of OA showed symptomatic improvement and delay in disease progression. Positive data showing dose-dependent decreases in the severity of cartilage and bone lesions following anterior cruciate ligament transection in rats were presented at the American College of Rheumatology ("ACR") Annual Meeting in November 2019. The preclinical data established a potentially safe and efficacious starting dose for a Phase 1 single ascending dose, or SAD, study which we initiated in March 2020.

The open-label, SAD study is designed to evaluate the safety and tolerability of three different doses (low, mid and high) of FX201 in cohorts of five to eight patients, with each patient receiving one injection. The initial trial is expected to enroll approximately 15 - 24 patients with symptomatic knee OA who will be followed for 104 weeks. Clinical data from the first two cohorts indicate that FX201 appears to be generally safe and well-tolerated at the low and mid doses. There were no serious adverse events and there was no evidence of systemic biodistribution in plasma or shedding in urine observed in any patient. In February 2021, following an independent Data Monitoring Committee (DMC) review of the mid dose safety data, we announced the expansion of the trial to include up to 20 additional patients in each of the low and mid dose treatment groups. In March 2021, the first patient was treated in the high dose cohort. Data through Week 52 for patients treated in the initial low and mid dose cohorts of the single ascending dose phase are expected by the end of 2021. In addition, preliminary data from the high dose cohort and expanded treatment groups are also anticipated before year-end.

FX201-Related Agreements

In December 2017, we acquired the global rights to develop and commercialize FX201 from GeneQuine Biotherapeutics GmbH, or GeneQuine and became the direct licensee of certain underlying Baylor patents and other proprietary rights related to FX201 for human applications. The Baylor license agreement grants us an exclusive, royalty-bearing, worldwide right and license (with a right to sublicense) for human applications under its patent and other proprietary rights related to FX201, with a similar non-exclusive license to certain Baylor intellectual property rights that are not specific to FX201. The license agreement with Baylor includes a low single-digit royalty on net sales of FX201 and requires us to use reasonable efforts to develop FX201 according to timelines set out in the license agreement. In December 2017, we entered into a Master Production Services Agreement with SAFC Carlsbad, Inc., a part of MilliporeSigma, for the manufacturing of preclinical and initial clinical supplies of FX201. In addition, in February 2020 we entered into a manufacturing agreement with another vendor for clinical trial supply of FX201 through potential Phase 3 clinical trials.

FX301

In September 2019, we acquired global rights to develop and commercialize XEN402, a NaV1.7 inhibitor known as funapide, from Xenon Pharmaceuticals Inc., or Xenon, for management of post-operative pain. FX301, an investigational NaV1.7 inhibitor product candidate consists of funapide formulated for extended release within a thermosensitive hydrogel, for local administration as a peripheral analgesic nerve block for control of post-operative pain. The proprietary formulation of the thermosensitive hydrogel was developed in our Innovation Lab. Approximately one minute following injection, the thermosensitive formulation has been shown to transition from a liquid to a gel, an effect that we believe can provide local, sustained delivery of funapide near target nerves for up to a week. Unlike typical local anesthetics, the selective pharmacology of funapide has the potential to provide effective non-opioid pain relief for at least 3-5 days, while preserving extremity motor function, which is typically compromised by local anesthetic peripheral nerve block. As such, we believe FX301 could enable ambulation, rapid discharge, and early rehabilitation following musculoskeletal surgery. In a validated post-operative pain model in pigs, FX301 administered as a peripheral nerve block demonstrated analgesic effect beginning at 1-hour post-dosing compared to placebo and significantly greater analgesic effect compared to liposomal bupivacaine at 36 hours post-dosing. Data from the study also indicated that treatment with FX301 did not significantly affect total walking distance in animals at 2 and 24 hours post-injection, whereas animals treated with liposomal bupivacaine experienced a significant reduction in total walking distance at those time points. Good Manufacturing Practice (GMP) manufacturing of clinical trial material and IND-enabling nonclinical studies are now complete. The FDA cleared our IND application in February 2021, and we plan to initiate a Phase 1b proof of concept clinical trial of popliteal fossa block (a commonly used nerve block in foot and ankle-related surgeries) with FX301 in patients undergoing bunionectomy. Results from the planned trial could potentially be available in late 2021.

FX301-Related Agreements

As part of the acquisition of rights from Xenon to develop and commercialize funapide, we became the direct licensee of certain underlying Xenon patents and other proprietary rights related to XEN402 for human applications. The Xenon agreement grants us an exclusive, royalty-bearing, world-wide right and license (with a right to sublicense) for human applications under its patents directly related to XEN402, with a similar royalty-free license to other Xenon proprietary rights directly related to XEN402.

Competition

Our industry is highly competitive and subject to rapid and significant technological change. The large size and expanding scope of the pain market makes it an attractive therapeutic area for biopharmaceutical businesses. Our potential competitors include pharmaceutical, biotechnology, medical device, and specialty pharmaceutical companies, including, but not limited to, Ampio Pharmaceuticals, Inc.; Anika Therapeutics, Inc.; Centrexion Therapeutics Corporation; Eli Lilly and Company; Kolon TissueGene, Inc.; Pfizer Inc.; Regeneron Pharmaceuticals, Inc.; Samumed, LLC; Taiwan Liposome Company; Teva Pharmaceutical Industries Ltd.; and Xalud Therapeutics, Inc. Several of these companies have robust drug pipelines, readily available capital, and established research and development organizations. We believe our success will be driven by our ability to develop and commercialize treatment options that make a meaningful difference for patients with musculoskeletal conditions, beginning with OA. The key competitive factors that could affect the success of our commercialization efforts are likely to be efficacy, safety, price, and the availability of reimbursement from government and other third-party payers.

ZILRETTA

Immediate-release steroids and HAs are currently the two marketed classes of IA products that compete directly with ZILRETTA. Also available are stem cell and platelet rich plasma, or PRP, injections, but these require on-site preparation from tissue or blood taken from the patient and have generated questionable efficacy in controlled clinical trials, and we believe they are unlikely to be a broadly embraced therapeutic option for OA patients. Because these are minimally manipulated autologous therapies, they do not require and have not received FDA review or approval. For that reason, they are generally not reimbursed by payers, and patients must pay out of pocket to receive these therapies. Furthermore, the American Association of Hip & Knee Surgeons issued a position statement indicating that it cannot recommend biologic therapies, including stem cell and PRP injections, for the treatment of advanced hip or knee arthritis. OARSI and ACR recently issued guidelines strongly recommending against use of IA stem cell therapy and PRP for the treatment of OA.

Intellectual Property/Patents and Proprietary Rights

We are building a broad, worldwide intellectual property portfolio to protect the proprietary position of ZILRETTA, our product candidates, and technology through a combination of patents, trade secrets, proprietary know-how, FDA exclusivity, and contractual restrictions on disclosure.

Patents and Patent Applications

We actively apply for, maintain, and plan to defend and enforce, as needed, our internally developed and externally licensed or acquired patent rights. Furthermore, we continue to search for and evaluate opportunities to in-license intellectual property relevant to our business.

ZILRETTA

We own three U.S. ZILRETTA patents as well as counterpart foreign patents and patent applications covering composition of matter, methods of manufacture, and methods of use. Our U.S. ZILRETTA patents have expiration dates in 2031. The ZILRETTA composition of matter invention is the result of several unique discoveries relating to a narrow drug load specification, a certain release profile of polymers, specific polymer weights and ratios, and clinical efficacy observed within a dose-range. The U.S. patents directed to ZILRETTA's composition of matter and methods of use are listed in the FDA Orange Book. We also have pending U.S. applications directed at compositions of matter similar to ZILRETTA, as well as methods of making and using the same, that, if resulting in an issued patent, could provide additional related claims expiring in 2031.

In 2020, we had additional patents granted in the EU, India, the Philippines, and the United States, further expanding our global intellectual property portfolio, which includes patents in Australia, Canada, China, Indonesia, Japan, Malaysia, Mexico, New Zealand, the Russian Federation, Saudi Arabia, Singapore, South Africa, South Korea, Taiwan, and Ukraine. These foreign patents cover the composition of matter, methods of manufacturing, and methods of using ZILRETTA and are similar in scope to the protection in the U.S. described above. In addition, we are continuing to prosecute our patent applications pending in additional countries throughout the world directed to ZILRETTA and related inventions.

We have also in-licensed intellectual property, owned by SwRI, which gives us exclusive rights to SwRI patents covering our proprietary microsphere manufacturing technology used in the production of ZILRETTA. These patents are scheduled to expire in 2025.

FX201

In December 2017, we acquired the global rights to FX201 from GeneQuine, including a direct exclusive license of certain foundational patents, patent applications, and other proprietary rights owned by Baylor that are related to FX201 for human applications. These patents generally cover the composition of matter and method of use of FX201 in the treatment of OA. In

2019, the U.S. PTO issued patent number 10,301,647, which covers the composition of matter and method of use of FX201 in the treatment of OA with a term through January 2033. In addition, the Baylor patents related to FX201 are issued in Europe, with an expiry date in 2032, and in Australia, Japan, China, India, and Eurasia with expiry dates in 2033. We are continuing to prosecute certain Baylor patent applications related to FX201. Further, we have a pending patent application covering composition of matter and effective dosages of FX201 in the treatment of OA in humans, which is expected to provide protection until 2039.

FX301

In September 2019, we acquired global rights to develop and commercialize funapide from Xenon, which we have formulated for extended release with our proprietary thermosensitive hydrogel as FX301. As part of the transaction with Xenon, we acquired foundational patents and patent applications covering the composition of matter, methods of use, and methods of manufacture related to funapide. We own patents directed to funapide granted in the U.S. as well as Australia, Canada, China, Europe, Hong Kong, Mexico and New Zealand with expiry dates in 2030. In addition, we have a pending patent application covering composition of matter, method of use, and method of manufacture for FX301, which is expected to provide protection until 2039.

Trade Secrets and Proprietary Information

The ZILRETTA microsphere PLGA formulation has been refined and optimized to deliver the drug substance released over an extended period of time. In developing this unique combination of manufacturing process and formulation, we have established numerous trade secrets, including those that relate to a precise pharmaceutical release profile. In addition, due to the complexity of the extended-release technology and the time, costs, and technical risks involved in demonstrating bioequivalence through clinical trials, we believe that the ability of manufacturers to gain market approval for generic alternatives to ZILRETTA upon expiration of our patents and FDA exclusivity will be challenging.

We seek to protect our proprietary information, including our trade secrets and proprietary know-how, by requiring our employees to execute a Proprietary Information, Inventions, Non-Solicitation, and Non-Competition Agreement upon the commencement of their employment. Consultants and other advisors are required to sign consulting agreements. These agreements generally provide that all confidential information developed or made known during the course of the relationship with us be kept confidential and not be disclosed to third parties except in specific circumstances. In the case of our employees, the agreements also typically provide that all inventions resulting from work performed for us, utilizing our property, or relating to our business and conceived or completed during employment shall be our exclusive property to the extent permitted by law. Further, we require confidentiality agreements from entities that receive our confidential data or materials.

Government Regulation and Product Approval

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

U.S. Biopharmaceutical Product Development Process

In the United States, the FDA regulates biopharmaceutical products under the Federal Food, Drug, and Cosmetic Act, or FDCA, the Public Health Service Act, or PHSA, and implementing regulations. Biopharmaceutical products are also subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable requirements at any time during the product development process, approval process or after approval, may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters, product recalls, product seizures, total or partial suspension of production or distribution injunctions, fines, refusals of government contracts, restitution, disgorgement of profits or civil or criminal penalties. The process required by the FDA before a biopharmaceutical product may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies according to Good Laboratory Practices, or GLP, or other applicable regulations;
- submission to the FDA of an investigational new drug, or IND, application, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, at each clinical site before each trial may be initiated;

- performance of adequate and well-controlled human clinical trials according to the FDA's laws and regulations pertaining to the conduct of human clinical studies, collectively referred to as Good Clinical Practices, or GCP, and according to the International Council for Harmonization, or ICH, GCP guidelines, to establish the safety and efficacy of the proposed biopharmaceutical product for its intended use;
- submission to the FDA of an NDA for a proposed new drug product or a Biologics License Application, or BLA, for a biological product;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the biopharmaceutical product is produced and tested to assess compliance with the FDA's cGMP requirements, to assure that the facilities, methods and controls are adequate to preserve the biopharmaceutical product's identity, strength, quality and purity;
- potential FDA audit of the non-clinical and clinical trial sites that generated the data in support of the NDA or BLA; and
- FDA review and approval or licensure of the NDA or BLA.

The lengthy process of seeking required approvals and the continuing need for compliance with applicable statutes and regulations require the expenditure of substantial resources and approvals are inherently uncertain.

Before testing any compounds with potential therapeutic value in humans, the biopharmaceutical product candidate enters the nonclinical testing stage, also referred to as preclinical testing. Preclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies to assess the potential safety and activity of the biopharmaceutical product candidate. The conduct of the preclinical tests must comply with federal regulations and requirements including GLP. The sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, among other documentation, to the FDA as part of the IND application. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA raises concerns or questions related to one or more proposed clinical trials and places the trial on a clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA may also impose clinical holds on a biopharmaceutical product candidate at any time before or during clinical trials due to safety concerns or non-compliance with applicable laws or regulations.

Clinical trials involve the administration of the biopharmaceutical product candidate to healthy subjects or patients with the target disease under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control. Clinical trials are conducted under written study protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety. Each protocol must be submitted to the FDA as part of the IND. Clinical trials must be conducted in accordance with the FDA's regulations which reflect the ICH GCP requirements. Further, each clinical trial must be reviewed and approved by an IRB at, or servicing, each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until it is completed.

Clinical trials for biopharmaceutical product candidates are typically conducted in humans in three sequential phases that may overlap. In Phase 1 clinical trials, the biopharmaceutical product is initially introduced into healthy human subjects and tested for safety or adverse effects, dosage, tolerance, metabolism, distribution, excretion and clinical pharmacology. In Phase 2 clinical trials, the biopharmaceutical product is evaluated in a limited patient population to identify possible adverse side effects and safety risks, evaluate preliminarily the efficacy of the biopharmaceutical product for specific targeted indications and determine dosage tolerance, optimal dosage and dosing schedule for patients having the specific disease. Once a biopharmaceutical product shows evidence of effectiveness and is found to have an acceptable safety profile in Phase 2 evaluations, Phase 3 clinical trials are undertaken to more fully evaluate clinical outcomes. In Phase 3 clinical trials, the biopharmaceutical product is administered to an expanded patient population in adequate and well-controlled trials to generate sufficient data to statistically confirm the efficacy and safety of the biopharmaceutical product for approval, to establish the overall risk-benefit profile of the biopharmaceutical product and to provide adequate information for its labeling.

Post-approval studies, also referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication and may be required by the FDA as part of the approval process.

Progress reports detailing the status of biopharmaceutical product development and results of the clinical trials must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected adverse events or any finding from tests in laboratory animals that suggests a significant risk for human subjects or patients. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any

specified period, if at all. The FDA or the sponsor or its data safety monitoring board (if applicable) may suspend a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the biopharmaceutical product has been associated with unexpected serious harm to study subjects.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the biopharmaceutical product as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the biopharmaceutical product candidate and, among other things, the manufacturer must develop methods for testing the safety, identity, strength, quality and purity of the final biopharmaceutical product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the biopharmaceutical product candidate does not undergo unacceptable deterioration over its shelf life.

FDA Review and Approval Processes

The results of product development, preclinical studies and clinical studies for claimed indications as well as descriptions of the manufacturing process and controls, analytical tests conducted on the biopharmaceutical product, proposed labeling and other relevant information are submitted to the FDA as part of an NDA or BLA requesting approval to market the product. A supplement to an approved NDA or BLA is also required to be submitted for review when seeking major changes to manufacturing or labeling, including additional indications for use. Additionally, the results of product development, preclinical studies and clinical trials for the claimed indications in all relevant pediatric subpopulations and the support for dosing and administration for each pediatric subpopulation for which the product is safe and effective, are contained in an NDA or BLA. The FDA may grant deferrals for submission of pediatric data or full or partial waivers after the initial submission of a pediatric study plan following an end of Phase 2 meeting unless otherwise agreed upon by the FDA and the sponsor. The submission of an NDA or BLA is subject to the payment of substantial user fees; a waiver of such fees may be obtained under certain limited circumstances.

The FDA reviews all NDAs and BLAs submitted before it accepts them for filing and may request additional information rather than accepting the application for filing. Once the application is accepted for filing, the FDA begins an in-depth review. Under the goals and policies agreed to by the FDA under the Prescription Drug User Fee Act, or PDUFA, the FDA has 12 months after submission for a new molecular entity in which to complete its initial review and respond to the applicant, and eight months for a priority review application. In addition, the FDA has 10 months after submission of an NDA for a non-new molecular entity in which to complete its initial review of a standard NDA and respond to the applicant, and six months for a priority review NDA. The FDA does not always meet its PDUFA goal dates for review of standard and priority review applications. The review process and the PDUFA goal date may be extended by additional three-month review periods whenever the FDA requests or the sponsor otherwise provides additional information or clarification regarding information already provided in the submission at any time during the review cycle.

The FDA reviews the NDA or BLA to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with cGMP to assure and preserve the product's identity, strength, quality and purity. The FDA may refer applications for novel biopharmaceutical products which present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. During the approval process, the FDA also will determine whether a risk evaluation and mitigation strategy, or REMS, is necessary to assure the safe use of the biopharmaceutical product. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS; the FDA will not approve the application without a REMS, if required.

Before approving an NDA or BLA, the FDA will typically inspect the facilities at which the product is to be manufactured. When an inspection is undertaken, the FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an application, the FDA will typically inspect one or more clinical sites to assure compliance with FDA regulations regarding conduct of clinical trials for the product's trials. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in a complete response letter to the applicant and often will request additional testing or information.

If a complete response letter is issued, the applicant may either resubmit the application, addressing all of the deficiencies identified in the letter, or withdraw the application.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling or REMS to assure safe use of the product through distribution or other controls. In addition, the FDA may require post approval studies, referred to as Phase 4 testing, which involves clinical trials designed to further assess a product's safety and effectiveness and may require testing and surveillance programs to monitor the safety of approved products that have been commercialized.

Post-Approval Requirements

Any products for which we receive FDA approval are subject to continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse experiences with the product, providing the FDA with updated safety and efficacy information, product sampling and distribution requirements, complying with certain electronic records and signature requirements and complying with FDA promotion and advertising requirements. These promotion and advertising requirements include, among other things, standards for direct-to-consumer advertising, prohibitions against promoting drugs for uses or in patient populations that are not described in the drug's approved labeling (known as "off-label use"), rules for conducting industry-sponsored scientific and educational activities, and promotional activities involving the internet. Failure to comply with FDA requirements can have negative consequences, including adverse publicity, enforcement letters from the FDA, mandated corrective advertising or communications with doctors, and civil or criminal penalties. Although physicians may prescribe legally available drugs for off-label uses, manufacturers may not market or promote such off-label uses.

We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products. Manufacturers of our products are required to comply with applicable FDA manufacturing requirements contained in the FDA's cGMP regulations. cGMP regulations require, among other things, quality control and quality assurance as well as the corresponding maintenance of records and documentation. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are also required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. Discovery of problems with a product after approval may result in restrictions on a product, manufacturer, or holder of an approved NDA. These restrictions may include suspension of a product until the FDA is assured that quality standards can be met, continuing oversight of manufacturing by the FDA under a consent decree of permanent injunction, which frequently includes the imposition of costs and continuing inspections over a period of many years, as well as possible withdrawal of the product from the market. In addition, changes to the manufacturing process generally require prior FDA approval before being implemented.

The FDA and other federal and state agencies closely regulate the promotion of drugs. Moreover, the FDA strictly regulates the promotional claims that may be made about drug and biologic products. In particular, a product may not be promoted for off label uses that are not approved by the FDA as reflected in the product's approved packaging label or are otherwise truthful and not misleading statements. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses.

Other types of changes to the approved product, such as adding new indications and additional labeling changes, are also subject to further FDA review and approval.

Pharmaceutical Coverage, Pricing, and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any biopharmaceutical product for which we obtain regulatory approval. In the United States and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend in part on the availability of coverage and adequate reimbursement from third-party payers.

In the United States, third-party payers include federal and state government payer programs, including Medicare and Medicaid, managed care organizations, private health insurers and other organizations. The process for determining whether a third-party payer will provide coverage for a drug product may be separate from the process for setting the price or reimbursement rate that the third-party payer will pay for the drug product. Third-party payers may limit coverage to specific drug products on an approved list, or formulary, which might not include all of the FDA-approved drug products for a particular indication. Third-party payers are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain FDA approvals. In addition, our biopharmaceutical products may not be considered medically necessary or cost-effective.

A third-party payer's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Further, one payer's determination to provide coverage for a drug product does not ensure that other payers also will provide coverage or an adequate reimbursement rate for the drug product. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

The cost of pharmaceuticals continues to generate substantial governmental and third-party payer scrutiny. We expect that the pharmaceutical industry will continue experiencing pricing pressures due to the trend toward managed healthcare, the increasing influence of managed care organizations and additional legislative proposals. Third-party payers are increasingly challenging the prices charged for medical products and services and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. If these third-party payers do not consider our products to be cost-effective compared to other available therapies, they may not cover our products after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products at a profit. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid healthcare costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. Adoption of such controls and measures and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceuticals such as the drug candidates that we are developing and could adversely affect our net revenue and results.

Different pricing and reimbursement schemes exist in other countries. In the European Community, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national healthcare systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost-effectiveness of a particular drug candidate to currently available therapies. Other member states allow companies to fix their own prices for medicines but monitor and control company profits. The downward pressure on healthcare costs in general, and on prescription drugs in particular, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country. There can be no assurance that any country that has price controls or reimbursement limitations for drug products will allow favorable reimbursement and pricing arrangements for any company.

Additionally, in order to be eligible for certain federal agencies and grantees to purchase ZILRETTA, or to have it paid for with federal funds under the Medicaid and Medicare Part B programs, we participate in the Department of Veterans Affairs, or VA, Federal Supply Schedule, or FSS, pricing program. We are obligated through the FSS program to sell ZILRETTA through an FSS contract and charge a price that is no higher than the statutory Federal Ceiling Price, or FCP, to four federal agencies (VA, U.S. Department of Defense, Public Health Service, and Coast Guard). The FCP is based on the non-federal Average Manufacturer Price, which we will need to calculate and report to the VA on a quarterly and annual basis. These obligations contain extensive disclosure and certification requirements.

Healthcare Reform

In the United States and foreign jurisdictions, there have been a number of legislative and regulatory changes to the healthcare system that could affect our future results of operations. In particular, there have been and continue to be a number of initiatives at the United States federal and state levels that seek to reduce healthcare costs, improve healthcare quality or expand access to healthcare.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, changed the way Medicare covers and pays for pharmaceutical products. The MMA expanded Medicare coverage to include outpatient prescription drug purchases made by the elderly by establishing Medicare Part D and introduced a new reimbursement methodology based on average sales prices for physician administered drugs under Medicare Part B. In addition, the MMA provided authority for limiting the number of drugs that would be covered in any therapeutic class under the Medicare Part D program. Cost reduction initiatives and other provisions of this legislation could decrease the coverage and reimbursement rate that we receive for ZILRETTA and any of our other approved products. While the MMA applies only to drug benefits for Medicare beneficiaries, private payers often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payers.

In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively PPACA, was enacted as a sweeping law intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements

for healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. Among the provisions of PPACA of importance to our potential drug candidates are the following:

- an annual, non-deductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;
- an increase in the rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for branded and generic drugs, respectively;
- 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;
- a new Medicare Part D coverage gap discount program, in which manufacturers must now agree to offer 70% point-of-sale discounts to negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the Federal Poverty Level, thereby potentially increasing manufacturers' Medicaid rebate liability;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements under the federal Open Payments program, created under Section 6002 of PPACA, and its implementing regulations, that manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) report annually to Centers for Medicare & Medicaid Services ("CMS") information related to "payments or other transfers of value" made or distributed to physicians, as defined by such law, and teaching hospitals (and, beginning in 2022, physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists, and certified nurse midwives), and that applicable manufacturers and applicable group purchasing organizations report annually to CMS ownership and investment interests held by physicians (as defined above) and their immediate family members;
- a requirement to annually report drug samples that manufacturers and distributors provide to physicians;
- expansion of healthcare fraud and abuse laws, including the federal False Claims Act and the federal Anti-Kickback Statute, new government investigative powers, and enhanced penalties for non-compliance;
- an FDA-approval framework for follow-on biologic products;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and
- establishment of a Center for Medicare & Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

There have been executive, judicial and Congressional challenges to numerous provisions of PPACA. For example, President Trump signed several Executive Orders and other directives designed to delay the implementation of certain provisions of PPACA or otherwise circumvent some of the requirements for health insurance mandated by PPACA. Concurrently, Congress considered legislation that would repeal or repeal and replace all or part of PPACA. While Congress has not passed comprehensive repeal legislation, several bills affecting the implementation of certain taxes under PPACA have been signed into law. The Tax Cuts and Jobs Act of 2017, or Tax Act, signed into law on December 22, 2017, includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by PPACA on certain individuals that fail to maintain qualifying health coverage for all of part of a year commonly referred to as the "individual mandate". In addition, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the PPACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminated the health insurer tax. The Bipartisan Budget Act of 2018, or the BBA, among other things, amended PPACA, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." On December 14, 2018, a Texas U.S. District Court Judge ruled that PPACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Act. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the PPACA are invalid as well. The U.S. Supreme Court is currently reviewing this case, but it is unknown when a decision will be reached. Although the U.S. Supreme Court has yet ruled on the constitutionality of the PPACA, on January 28, 2021, President Biden issued an

executive order to initiate a special enrollment period from February 15, 2021, through May 15, 2021, for purposes of obtaining health insurance coverage through the PPACA marketplace. The executive order also instructs certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the PPACA. It is unclear how the Supreme Court ruling, other such litigation, and the healthcare reform measures of the Biden administration will impact PPACA.

In addition, since the PPACA was enacted, other legislative changes have been proposed and adopted that may impact the extent to which we are able to successfully commercialize any of our product candidates that receive regulatory approval. For example, in August 2011, then-President Obama signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals in spending reductions. The Joint Select Committee on Deficit Reduction did not achieve a targeted deficit reduction, which triggered the legislation's automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of, on average, two percent per fiscal year through 2030 unless Congress takes additional action. However, COVID-19 relief support legislation suspended the 2% Medicare sequester from May 1, 2020, through March 31, 2021.The American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several providers, including hospitals and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices, including at the federal level several recent U.S. Congressional inquiries and legislation designed to, among other things, increase drug pricing transparency, reduce the cost of drugs under Medicare, review relationships between pricing and manufacturer patient assistance programs, and reform government program drug reimbursement methodologies. At the federal level, the Trump administration used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. For example, on July 24, 2020, and September 13, 2020, the Trump administration announced several executive orders related to prescription drug pricing that attempt to implement several of the administration's proposals. The FDA also released a final rule, effective November 30, 2020, implementing a portion of the importation executive order providing guidance for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022, to January 1, 2023, in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed pending review by the Biden administration until March 22, 2021. On November 20, 2020, CMS issued an interim final rule implementing President Trump's Most Favored Nation executive order, which would tie Medicare Part B payments for certain physician-administered drugs to the lowest price paid in other economically advanced countries, effective January 1, 2021. On December 28, 2020, the United States District Court in Northern California issued a nationwide preliminary injunction against implementation of the interim final rule. However, it is unclear whether the Biden administration will work to reverse these measures or pursue similar policy initiatives. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, to encourage importation from other countries and bulk purchasing. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize ZILRETTA and any future products for which we receive regulatory approval.

We expect that PPACA reform, as well as other healthcare reform measures that have been and may be adopted in the future, may result in more rigorous coverage criteria and lower reimbursement, as well as additional downward pressure on the price that we receive for any approved product, including ZILRETTA.

Regenerative Medicine Advanced Therapies

As part of the 21st Century Cures Act, Congress amended the FDCA to create the regenerative medicine advanced therapies, or RMAT, designation. The RMAT designation is intended to facilitate efficient development and expedite review of regenerative medicine advanced therapies, which are intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition. RMAT covers cell therapies, gene therapies, therapeutic tissue engineering products, human cell and tissue products, and combination products using any such therapies or products. A sponsor may request that the FDA designate a regenerative medicine advanced therapy concurrently with or at any time after submission of an IND. The FDA has 60 calendar days to determine whether the criteria are met, including whether there is preliminary clinical evidence indicating the potential to address unmet medical needs for a serious or life-threatening disease or condition. A BLA for a

regenerative medicine advanced therapy may be eligible for priority review or accelerated approval through surrogate or intermediate endpoints reasonably likely to predict long-term clinical benefit, or reliance upon data obtained from a meaningful number of clinical trial sites. Benefits of such designation also include early interactions with the FDA to discuss any potential surrogate or intermediate endpoint to be used to support accelerated approval. A regenerative medicine advanced therapy that is granted accelerated approval and is subject to post-approval requirements may fulfill such requirements through the submission of clinical evidence, clinical studies, patient registries, or other sources of real-world evidence, such as electronic health records; the collection of larger confirmatory data sets; or post-approval monitoring of all patients treated with such therapy prior to its approval.

Other U.S. Healthcare Laws and Compliance Requirements

In the United States, our activities are subject to regulation by various federal, state and local authorities in addition to the FDA, including CMS, other divisions of HHS (*e.g.*, the Office of Inspector General), the United States Department of Justice and individual United States Attorney offices within the Department of Justice, and state and local governments. For example, various activities, including but not limited to sales, marketing and scientific/educational grant programs, must comply with the anti-fraud and abuse provisions of the Social Security Act, the federal Anti-Kickback Statute, the federal False Claims Act and similar state laws, each as amended. Failure to comply with such requirements could potentially result in substantial penalties to us. Even if we structure our programs with the intent of compliance with such laws, there can be no certainty that we would not need to defend against enforcement or litigation, in light of the fact that there is significant enforcement interest in pharmaceutical companies in the United States, and some of the applicable laws are quite broad in scope.

The federal Anti-Kickback Statute prohibits any person or entity, including a prescription drug manufacturer (or a party acting on its behalf), from knowingly and willfully soliciting, receiving, offering or providing remuneration, directly or indirectly, to induce or reward either the referral of business, or the furnishing, recommending, or arranging for the purchase, lease or order of a good, facility, item or service, for which payment may be made under a federal healthcare program, such as the Medicare or Medicaid program. This statute has been interpreted broadly to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers, and formulary managers, among others, on the other. The term “remuneration” has been broadly interpreted to include anything of value, including for example, gifts, discounts, the furnishing of supplies or equipment, credit arrangements, payments of cash, waivers of payments, ownership interests and providing anything at less than its fair market value.

Federal false claims and false statements laws, including the federal False Claims Act, prohibit, among other things, any person or entity from knowingly presenting, or causing to be presented, a false or fraudulent claim for items or services, including drugs, for payment to, or approval by, a federal healthcare program, including Medicare or Medicaid. The qui tam provisions of the federal False Claims Act allow a private individual to bring a civil action on behalf of the federal government alleging that the defendant has submitted a false claim to the federal government, and to share in any monetary recovery. In recent years, the number of suits brought by private individuals has increased dramatically.

The Health Insurance Portability and Accountability Act of 1996, or HIPAA, created several new federal crimes, including healthcare fraud and false statements relating to healthcare matters. The healthcare fraud statute prohibits knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including third-party payers. The false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services.

The 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 report annually to CMS information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Beginning in 2022, applicable manufacturers also will be required to report such information regarding its payments and other transfers of value to physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists and certified nurse midwives during the previous year.

Also, many states have similar laws and regulations, such as anti-kickback and false claims laws that may be broader in scope and may apply regardless of payer, in addition to items and services reimbursed under Medicaid and other state programs. Additionally, we may be subject to state laws that require pharmaceutical companies to comply with the federal government’s and/or pharmaceutical industry’s voluntary compliance guidelines, state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures, as well as state and foreign laws governing the privacy and security of health information, many of which differ from each other in significant ways and often are not preempted by HIPAA.

HIPAA, as amended by the Health Information Technology and Clinical Health Act of 2009, and their respective implementing regulations, impose requirements on certain healthcare providers, health plans, and healthcare clearinghouses, known as covered entities, and their business associates and covered subcontractors that perform services involving the use or disclosure of individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information.

Where our activities involve foreign government officials, they may also potentially be subject to the Foreign Corrupt Practices Act, which prohibits companies and individuals from engaging in specified activities to obtain or retain business or to influence a person working in an official capacity. Under the FCPA, it is illegal to pay, offer to pay, or authorize the payment of anything of value to any foreign government official, governmental staff members, political party or political candidate in an attempt to obtain or retain business or to otherwise influence a person working in an official capacity. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the corporation and to devise and maintain an adequate system of internal accounting controls.

If we seek to have a product covered in the United States by the Medicaid programs, various obligations, including government price reporting, are required under the Medicaid rebate requirements of the Omnibus Budget Reconciliation Act of 1990 and the Veterans Health Care Act of 1992, each as amended, which generally require products to be offered at substantial rebates/discounts to such programs and certain purchasers. In order to distribute products commercially, we must comply with state laws that require the registration of manufacturers and wholesale distributors of pharmaceutical products in a state, including, in certain states, manufacturers and distributors who ship products into the state even if such manufacturers or distributors have no place of business within the state. Some states also impose requirements on manufacturers and distributors to establish the pedigree of product in the chain of distribution, including some states that require manufacturers and others to adopt new technology capable of tracking and tracing product as it moves through the distribution chain. Many of our current as well as possible future activities are potentially subject to federal and state consumer protection and unfair competition laws. We must also comply with laws that require clinical trial registration and reporting of clinical trial results on the publicly available clinical trial databank maintained by the National Institutes of Health at www.ClinicalTrials.gov. We are subject to various environmental, health and safety regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous substances. From time to time, and in the future, our operations may involve the use of hazardous materials.

To the extent that any of our products are sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

U.S. Marketing Exclusivity

Hatch-Waxman Exclusivity.

Market exclusivity provisions under the FDCA can delay the submission or approval of certain applications of other companies seeking to reference another company's NDA. If the new drug is a new chemical entity subject to an NDA, the FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to obtain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application, or ANDA, or a Section 505(b)(2) NDA submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, such an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator NDA holder. The FDCA also provides three years of marketing exclusivity for an NDA, or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the conditions associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Rest of World Government Regulation

In addition to regulations in the United States, we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of our future products.

Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application much like the IND prior to the commencement of human clinical trials.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Employees and Human Capital

As of December 31, 2020, we had 257 full-time employees, of which 254 were based in the United States. Of the total employees, 154 were in our commercial group, 63 were in research and development, and 40 were in general and administrative roles. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

At Flexion, we strive for inclusion, prize ingenuity, and see our mission as advancing medicines that matter to patients in need. Our values—focus, ingenuity, tenacity, transparency, and fun—form the fabric of the organization, are reinforced daily, and become key dimensions in the hiring and performance process as we continuously strive to make Flexion a magnet for outstanding talent and a great place to work.

We promote an environment of diversity and inclusiveness at Flexion, regardless of race, gender, sexual orientation, religion, ethnicity, national origin, physical disability or age. We continue to educate ourselves through our engagement with a Diversity, Equity and Inclusion (DEI) consultant, and are working to ensure that DEI will become progressively engrained into the fabric of the Flexion organization. In August 2020, as a testament to our commitment, our CEO signed the MassBio CEO Pledge for a More Equitable and Inclusive Life Sciences Industry, on behalf of our Executive Committee and our entire company. As of December 31, 2020, over half of our workforce was female, and we are committed to recruitment and promotion of underrepresented communities.

We seek to attract, engage, and motivate top talent through an innovative, market-leading total rewards portfolio that includes wellness programs, a bi-annual survey on benefits satisfaction, recognition programs, rewards for high performers and high potentials, a competitive PTO policy, unlimited sick time, and flexible work-from-home guidelines, and we seek to provide a desirable work/life balance. We partner with a leading compensation consulting firm to ensure accurate industry benchmarking and review our compensation each year to ensure pay equity across various categories. We offer differentiated and targeted learning and development options for employees at all levels, including on-the-job training, coaching engagements, mentoring, internal training workshops, and external training opportunities.

We conduct a comprehensive annual and short, bi-weekly surveys to evaluate engagement, with high participation rates and scores, and we work with an external review site that provides confidential company ratings from employees on leadership, compensation, teamwork, environment, and outlook. In the most recent survey, we received an A+ rating overall as well as across more than 15 different categories. We were one of Boston Business Journal’s Best Places to Work in 2017, 2018, and 2019, and in 2019 were the only Boston-area biopharmaceutical company recognized in the medium business category (100-249 employees).

Corporate Citizenship

We are dedicated to the principles of environmental stewardship, social responsibility, and good corporate governance. Our Board of Directors is comprised of industry leaders with extensive and diverse experience spanning business and scientific leadership. We hold ourselves to the highest standards and our Code of Business Conduct and Ethics reflects the business practices and principles of behavior that support this commitment. We are deeply invested in the welfare of patients, employees, the environment and the communities where we live and work. We conduct our operations and manage our product and pipeline programs in a responsible manner and strive to comply with applicable laws, rules and regulations.

From a social responsibility perspective, we are focused on making a meaningful difference in the lives of people living with musculoskeletal conditions, like OA. Through our extensive knowledge, expertise and capabilities in the development and commercialization of novel, local therapies, we aim to realize the greatest value for patients, employees and communities. We provide funding to non-profit patient advocacy organizations like the Arthritis Foundation and Osteoarthritis Action Alliance, as well as sponsor a Corporate Work Study Program for students attending Notre Dame Cristo Rey High School, a non-profit organization committed to providing affordable, culturally sensitive, college preparatory education enhanced by professional work experience for young men and women from families with limited income. Also, in response to the COVID-19 pandemic, we donated personal protection equipment from our Innovation Lab to local hospitals and to the collection effort coordinated by MassBio to help with the increased demand for medical supplies.

As it relates to being an environmentally responsible member of our community, we adhere to Good Manufacturing Practice (GMP) guidelines as set forth by the FDA to ensure our product and drug candidates are consistently produced and controlled according to quality standards. We also proactively look for opportunities to reduce waste and employ green technology wherever possible. In 2018 we installed water filtration coolers to dramatically decrease the use of plastic bottles. The building in which we are headquartered was granted an ENERGY STAR certification by the Environmental Protection Agency in 2020 and employs single-stream recycling. In addition, at both our main office and our Innovation Laboratory we utilize automated lighting controls and 100% recycled paper goods.

As we continue to build our company, we will keep environmental, social and governance considerations at the forefront of our efforts.

Research and Development

We invested $54.3 million, $69.6 million, and $53.1 million in research and development in the years ended December 31, 2020, 2019, and 2018, respectively.

Corporate and Other Information

We were incorporated in Delaware in November 2007. Our principal executive offices are located at 10 Mall Road, Suite 301, Burlington, Massachusetts 01803, and our telephone number is (781) 305-7777. Our corporate website address is www.flexiontherapeutics.com. Information contained on or accessible through our website is not a part of this Annual Report, and the inclusion of our website address in this Annual Report is an inactive textual reference only. Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and amendments to reports filed pursuant to Sections 13(a) and 15(d) of the Exchange Act are available free of charge on our website as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. We also regularly post copies of our press releases as well as copies of presentations and other updates about our business on our website at www.flexiontherapeutics.com. Information contained in our website does not constitute a part of this Annual Report or our other filings with the SEC. The SEC maintains an internet site that contains our public filings with the SEC and other information regarding our company, at www.sec.gov.

This Annual Report contains references to our trademarks and to trademarks belonging to other entities. Solely for convenience, trademarks and trade names referred to in this Form 10-K, including logos, artwork and other visual displays, may appear without the ® or TM symbols, but such references are not intended to indicate, in any way, that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto. We do not intend our use or display of other companies' trade names or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other companies.

ITEM 1A. RISK FACTORS

Risk Factors Summary:

The summary of risks below provides an overview of the principal risks we are exposed to in the normal course of our business activities:

- We have incurred and expect to incur significant losses, our revenues may not be sufficient to cover our future expenses, and we may never be profitable.
- Failure to obtain additional financing could significantly harm our business.
- COVID-19 may continue to adversely impact our business and results of operations.
- Our prospects are highly dependent on the successful commercialization of our sole product, ZILRETTA, and failure to develop, acquire, or in-license other products or product candidates, will limit our business and prospects.
- We may be unable to remove the LOU or expand the label for ZILRETTA and may never obtain regulatory approval of ZILRETTA for additional indications, of our other product candidates in the United States, or of ZILRETTA or our product candidates outside of the United States, which would limit our ability to realize their full market potential.
- Successful commercialization of any product we may offer depends on our ability to differentiate it from existing therapies; maintain our sales and marketing capabilities; train and equip our sales force; enter into agreements with third parties that satisfactorily market, distribute, or sell that product; and obtain adequate third-party payer coverage and reimbursement and will be adversely impacted by unfavorable third-party guidelines or recommendations and any generic competition.

- Our clinical development efforts depend on the satisfactory performance by third parties on which we rely in conducting our preclinical studies and clinical trials and will take a long time, be subject to delays, be expensive, and may ultimately prove unsuccessful.
- We rely completely on a limited number of third parties, including certain sole sources of supply, to manufacture our commercial supplies of ZILRETTA and our preclinical and clinical drug supplies for our product candidates, and any failure on their part could impact our sales, research and development, and regulatory approval efforts and increase our costs.
- We may not be successful in establishing and maintaining effective development and commercialization collaborations, and our partners may fail in development or commercialization efforts, which could adversely affect our ability to develop or commercialize products and our financial condition and operating results.
- Our clinical study results do not guarantee similar efficacy following commercialization.
- The regulatory approval process for our product candidates is lengthy, time-consuming, and unpredictable.
- We are subject to substantial ongoing regulatory requirements and may face development and regulatory difficulties.
- Relationships with healthcare professionals, clinical investigators, consultants, actual and potential customers, and third-party payers are and will continue to be subject to healthcare laws.
- New legislation may increase the difficulty and cost for us to commercialize any product we may offer, affect the prices we may obtain, and increase the time, effort, and cost involved in regulatory compliance.
- We could face liability if a regulatory authority determines that we are promoting a product for any off-label uses.
- We may be unable to adequately protect or enforce our intellectual property rights and face ongoing risks from patent litigation, allegations by third parties that we are infringing their intellectual property rights, and claims of breach of intellectual property licensing agreements or confidentiality obligations.
- We face significant competition, including from well-established biopharmaceutical companies, which may harm our business.
- We may not be able to retain key executives and to attract, retain, and motivate qualified personnel.
- We are at risk of product liability claims, general and securities class action litigation, and penalties associated with regulatory enforcement.
- Failure to comply with applicable privacy and data protection laws and regulations may subject us to liabilities that adversely affect our business, operations, and financial performance.
- We are subject to a variety of risks associated with international operations, including geopolitical events, pandemics, natural disasters, and foreign exchange rates.
- Failure, inadequacy, interruption, or security lapse of our information technology could harm our ability to operate our business effectively and subject us to liability.
- The market price of our common stock may be highly volatile and is subject to substantial sales of shares of our common stock by our stockholders or our sale of securities to fund our operations, which may also dilute our stockholders and impose additional restrictions on our business.
- We do not intend to pay dividends on our common stock, so any returns will be limited to the value of our stock.
- Failure to maintain effective internal controls over financial reporting may lead to inaccurate reports of our financial results or allow fraud, which could harm our business and the trading price of our common stock.
- Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.
- Provisions in our organization documents and Delaware law could make it more difficult for a third party to acquire us and may prevent or frustrate attempts by our stockholders to replace or remove our current management.

Risk Factors:

You should consider carefully the risks described below, together with the other information contained in this Annual Report on Form 10-K and other documents we file with the Securities and Exchange Commission. The risks and uncertainties below are those identified by us as material, but there are also additional risks and uncertainties that we are unaware of that may become important factors that affect us. If any of the following risks occurs, our business, financial condition, results of operations, and future growth prospects would likely be materially and adversely affected, and the market price of our common stock would likely decline.

Risks Related to Our Financial Condition and Need for Additional Capital

We have incurred significant losses since our inception and anticipate that we will continue to incur significant losses over the next few years.

We have a limited operating history. To date, we have focused primarily on developing our commercialized product, ZILRETTA. Our current and future product candidates will require substantial development time and resources before we would be able to apply for or receive regulatory approvals and begin generating revenue from product sales. We have incurred significant net losses in each year since our inception, including significant net losses in each of the three immediately preceding years, and expect to incur net losses over the next few years as we continue to invest in the commercialization of ZILRETTA and advance our development programs.

We have devoted most of our financial resources to product development and commercialization. To date, we have financed our operations almost exclusively through the sale of equity securities and debt. The size of our future net losses will depend, in part, on the rate of future expenditures and our ability to generate revenue. We launched commercial sales of ZILRETTA in the fourth quarter of 2017, and, in light of our limited commercial history, cannot guarantee that our commercialization efforts will result in product revenues that meet our peak sales expectations or those of analysts and investors.

Since first reported in December 2019, the novel strain of coronavirus that causes the COVID-19 disease ("COVID-19") has become a global pandemic. Many governments have implemented various "social distancing" and "stay at home" measures to mitigate the continued spread of COVID-19. ZILRETTA is required to be administered by healthcare professionals, and, since mid-March 2020, COVID-19 has resulted in limited patient access to physician offices and clinics as healthcare practices have implemented varying responses to the pandemic. Although many practices have reopened, some have limited in-person patient visits. In addition, we believe that many patients have been reluctant to visit physician offices and clinics due to fear of contracting COVID-19. While COVID-19 vaccines, which were first introduced in December 2020, will likely moderate these effects on patient visit rates over time, patients' ability to access and willingness to use these vaccines, the degree of vaccine efficacy, and the emergence of new viral strains will influence the rate of change, and restrictions on the administration of other medicines, including ZILRETTA, within a number of days of a COVID-19 vaccination may further reduce the frequency of ZILRETTA's administration. As a result of these adverse impacts on the operations of healthcare providers who administer ZILRETTA to patients and patients' willingness to make in-person visits to healthcare facilities, we have experienced and, in combination with restrictions associated with COVID-19 vaccine administration, may continue experiencing a meaningful diminution in revenue as compared to our prior expectations.

We also expect to continue to incur substantial expenses as we invest in the further commercialization of ZILRETTA, further scale up commercial manufacturing of ZILRETTA, conduct additional clinical trials for it and our product candidates, and continue our development activities with respect to our product pipeline. As a result, we expect to continue to incur significant losses and negative cash flows over the next few years.

Our revenues may not be sufficient to cover our future expenses, and we may never be profitable.

Our ability to generate significant revenue and achieve profitability depends primarily on our ability to successfully commercialize ZILRETTA and to obtain regulatory approval for and then successfully commercialize our product candidates. We may never succeed in these activities and may never generate revenues that are significant enough to achieve profitability.

Because of the numerous risks and uncertainties associated with new pharmaceutical products and development efforts, we are unable to predict the timing or amount of increased expenses; when, or if, we will begin to generate revenue from product sales sufficient to cover our operating expenses; or when, or if, we will be able to achieve or maintain profitability. In addition, despite actions aimed at reducing our operating expenses, our expenses could increase beyond expectations if we determine that additional sales and marketing personnel or other resources are necessary for successful commercialization, if we face any legal or regulatory action related to our commercial activities, or if our development expenses for our product candidates are greater than we expect.

If we are unable to generate sufficient revenues from product sales or to maintain an acceptable cost structure related to our operations, we may not become profitable and may need to obtain additional funding to continue operations.

If we fail to obtain additional financing, we may be forced to delay, reduce, or eliminate our product development programs and commercialization activities.

Developing and commercializing pharmaceutical products, including conducting preclinical studies and clinical trials, and building and maintaining sales and marketing capabilities, is expensive. Changing circumstances may cause us to consume capital more rapidly than we currently anticipate.

Attempting to secure additional financing may divert our management from our day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. In particular, as a result of COVID-19 and actions taken to slow its spread, the global credit and financial markets have experienced extreme volatility and disruptions, including diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates, and uncertainty about economic stability. These factors may make any additional debt or equity financing more difficult, more costly, and more dilutive. Inability to raise additional capital when required or on acceptable terms may require us to:

- significantly scale back or discontinue our commercialization efforts or the further development of our product candidates;
- seek corporate partners for our product candidates at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available;
- seek corporate partners to assist in commercialization on terms that are less favorable than might otherwise be available;
- relinquish, or license on unfavorable terms, our rights to products or product candidates that we otherwise would seek to develop or commercialize ourselves; or
- significantly curtail, or cease, operations.

We may sell additional equity or debt securities to fund our operations, which may result in dilution to our stockholders and impose restrictions on our business.

In order to raise additional funds to support our operations, we may sell additional equity or debt securities, which could adversely impact our stockholders as well as our business. The sale of additional equity or convertible debt securities would result in the issuance of additional shares of our capital stock and dilution to all of our stockholders. The incurrence of debt would result in increased fixed payment obligations and could also result in certain restrictive covenants—such as limitations on our ability to incur additional debt or acquire, sell, or license intellectual property rights—that would adversely impact our ability to conduct business.

Our existing indebtedness contains restrictions that limit our flexibility in operating our business. In addition, we may be required to make a prepayment or repay our outstanding indebtedness earlier than we expect.

On August 2, 2019, we entered into an Amended and Restated Credit and Security Agreement with Silicon Valley Bank, MidCap Financial Trust, and Flexpoint MCLS Holdings, LLC, or the Credit Agreement, which provides for a term loan of $40.0 million and a revolving credit facility up to $20.0 million. We concurrently drew down the $40.0 million term loan and used $7.7 million of the proceeds to repay the remaining amount owed on our prior credit facility. In February 2020, we drew down $20.0 million from the revolving credit facility. On May 18, 2020, we entered into an amendment to the Credit Agreement pursuant to which we borrowed $15.0 million under a new term loan advance and immediately used the proceeds to repay an equal amount under the revolving credit facility, and the maximum principal amount of the revolving credit facility was reduced from $20.0 million to $5.0 million. The new term loan is subject to substantially the same terms, including interest rate, amortization, and maturity date, as the existing term loan under the credit facility. The Credit Agreement contains various covenants that limit our ability to engage in specified types of transactions. These covenants limit our ability to, among other things:

- incur or assume certain debt;
- merge or consolidate or acquire all or substantially all of the capital stock or property of another entity;
- enter into any transaction or series of related transactions that would be deemed to result in a change in control of us under the terms of the agreement;
- change the nature of our business;
- change our organizational structure or type;
- amend, modify, or waive any of our organizational documents;
- license, transfer, or dispose of certain assets;
- grant certain types of liens on our assets;
- make certain investments;
- pay cash dividends;
- enter into material transactions with affiliates; and

- amend or waive provisions of material agreements in certain manners.

Under the Credit Agreement, as amended, we are subject to a minimum liquidity threshold, such that at any time our liquidity is below $80.0 million, we will become subject to a minimum revenue covenant. The minimum liquidity threshold includes certain accounts receivable as deemed eligible under the Credit Agreement, in addition to cash, cash equivalents, and marketable securities. Prior to May 2021, the minimum revenue covenant, if it applies in the future, is unmodified and is based on the greater of (i) a conservative percentage of the year's approved forecast and (ii) modest growth over the trailing twelve months of actual revenues. Beginning in May 2021, the minimum revenue covenant, if it applies, will be the greatest of (i) a conservative percentage of the year's approved forecast, (ii) modest growth over the trailing twelve months of actual revenues and (iii) 100% of the minimum revenue covenant amount for the preceding month.

If the revenue covenant becomes applicable to us and we fail to meet it, the commitments under the Credit Agreement could be terminated and any outstanding borrowings, together with accrued interest, under the Credit Agreement could be declared immediately due and payable. Additionally, if our liquidity is below $80.0 million, all amounts received from customer collections will be applied immediately to reduce the revolving credit facility. The restrictive covenants in the Credit Agreement could prevent us from pursuing business opportunities that we or our stockholders may consider beneficial.

A breach of any of these covenants could result in an event of default under the Credit Agreement. An event of default will also occur if, among other things, a material adverse change in our business, operations, or condition occurs, which could potentially include a material impairment of the prospect of our repayment of any portion of the amounts we owe under the Credit Agreement. In the case of a continuing event of default under the Credit Agreement, the lenders could elect to declare all amounts outstanding to be immediately due and payable, proceed against the collateral in which we granted the lenders a security interest under the Credit Agreement, or otherwise exercise the rights of a secured creditor. Amounts outstanding under the Credit Agreement are secured by all of our existing and future assets, excluding intellectual property, which is subject to a negative pledge arrangement.

In April 2017, we also issued $201.3 million principal amount of our 3.375% Convertible Senior Notes due 2024, or the 2024 Convertible Notes. The 2024 Convertible Notes will mature on May 1, 2024, unless earlier redeemed, repurchased, or converted in accordance with the terms of the indenture governing the notes. If specified bankruptcy, insolvency, or reorganization-related events of default occur, or if certain other events of default occur, including a default under the Credit Agreement resulting in an obligation to repay the indebtedness, and the trustee or certain holders of the 2024 Convertible Notes elect, the principal of, and accrued and unpaid interest on, all of the then-outstanding 2024 Convertible Notes will automatically become due and payable. In addition, if we undergo certain fundamental change transactions specified in the indenture governing the 2024 Convertible Notes, the holders of the notes may require us to repurchase their notes at a price equal to 100% of the principal amount of the notes, plus any accrued and unpaid interest.

We may not have enough available cash or be able to raise additional funds on satisfactory terms, if at all, through equity or debt financings to repay or refinance our indebtedness at the time any such repayment or repurchase is required. In such an event, we may be required to delay, limit, reduce, or terminate our product development or commercialization efforts or grant others rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. Our business, financial condition, and results of operations could be materially adversely affected as a result.

Risks Related to Commercialization Activities

Our prospects are highly dependent on the successful commercialization of ZILRETTA. To the extent ZILRETTA is not commercially successful, our business, financial condition, and results of operations may be materially adversely affected.

ZILRETTA is our only drug that has been approved for sale, and it has only been approved for the management of OA pain of the knee for patients in the United States. We are focusing a significant portion of our activities and resources on ZILRETTA, and we believe our prospects are highly dependent on, and a significant portion of the value of our company relates to, our ability to successfully commercialize ZILRETTA in the United States.

Successful commercialization of ZILRETTA is subject to many risks. We have never, as an organization, commercialized a product prior to ZILRETTA, and there is no guarantee that we will be able to do so successfully with ZILRETTA for its approved indication. There are numerous examples of failures to meet expectations of market potential, including by pharmaceutical companies with more experience and resources than us.

Market acceptance of ZILRETTA and any other product for which we receive approval will depend on a number of factors, including:

- the efficacy and safety as demonstrated in clinical trials;
- the ability to demonstrate the impact of real-world evidence;
- the timing and market introduction of competitive products;

- the product label and clinical indications for which the product is approved;
- acceptance by physicians, the medical community, and patients of the product as a safe and effective treatment;
- the ability to distinguish safety and efficacy from existing, less expensive generic alternative therapies;
- the convenience of prescribing, administrating, and initiating patients on the product;
- the potential and perceived advantages or value of the product over alternative treatments;
- the cost of treatment in relation to alternative treatments, including any similar generic treatments;
- the economics of a buy-and-bill product and discounts and rebates we offer;
- the availability of coverage and adequate reimbursement by third-party payers and government authorities to support pricing;
- the prevalence and severity of adverse side effects; and
- the effectiveness of sales and marketing efforts.

COVID-19 has adversely impacted our commercialization of ZILRETTA.

COVID-19 has severely impacted our commercialization of ZILRETTA. For example, federal, state, and local governments have taken varying preventive and proactive measures to slow the spread of COVID-19. While some healthcare facilities and physician offices, particularly those in major markets, have reopened and rescheduled previously cancelled or postponed non-emergency or elective procedures, COVID-19 cases have increased, and new viral strains have emerged, which may result in additional delays in procedures or otherwise restricted patient visits. Even in those markets where facilities are operating with fewer restrictions, we believe patients continue to be reluctant to seek treatment for fear of contracting COVID-19. These impediments and disruptions in patient care have resulted in a decreased volume of ZILRETTA being administered, which has translated into decreased sales.

As the COVID-19 pandemic continues to evolve, we are uncertain as to whether states may implement new measures or how healthcare practices will respond. Even in those regions where healthcare operations and patient visits have fully resumed, we expect that it will take some time for activities to return to levels seen before the pandemic. While COVID-19 vaccines, which were first introduced in December 2020, will likely moderate these effects on patient visit rates over time, patients' ability to access and willingness to use these vaccines, the degree of vaccine efficacy, and the emergence of new viral strains will influence the rate of change, and restrictions on the administration of other medicines, including ZILRETTA, within a number of days of a COVID-19 vaccination may further reduce the frequency of ZILRETTA's administration. We expect sales of ZILRETTA to continue to be negatively impacted for the foreseeable future until the effects of COVID-19 are fully resolved. It is also possible that a prolonged impact of COVID-19 and the associated reduction of physician office visits could force various healthcare practices, particularly smaller primary care or orthopedic practices, to permanently close or to consolidate with larger practices or healthcare groups, which could cause us to lose previously established physician relationships and set back our efforts to increase adoption of ZILRETTA.

If we are unable to differentiate ZILRETTA from existing generic therapies for the treatment of OA, or if the FDA or other applicable regulatory authorities approve generic products that compete with ZILRETTA, our ability to successfully commercialize ZILRETTA would be adversely affected.

Immediate-release TA and other injectable immediate-release steroids, which are the current intra-articular, or IA, standard of care for OA pain, are available in generic form and are therefore relatively inexpensive compared to the pricing for ZILRETTA. These generic steroids also have well-established market positions and familiarity with physicians, healthcare payers, and patients. Although we believe the proven and extended pain relief evidenced in our clinical trials demonstrate that ZILRETTA represents a clinically meaningful and highly efficacious option, it is possible that we will receive data from additional clinical trials or in a post-marketing setting from physician and patient experiences with the commercial product that does not continue to support such interpretations. It is also possible that the FDA, physicians and healthcare payers will not agree with our interpretation of our existing and future clinical trial data. If we are unable to demonstrate the value of ZILRETTA based on our clinical data, patient experience, as well as real-world evidence, our opportunity for ZILRETTA to maintain premium pricing and be commercialized successfully would be adversely affected.

In addition to existing generic steroids, such as immediate-release TA, the FDA or other applicable regulatory authorities may approve other generic products that could compete with ZILRETTA if we cannot adequately protect it with our patent portfolio. Once an NDA, including a Section 505(b)(2) application, is approved, the product covered thereby becomes a "listed drug," which can, in turn, be cited by potential competitors in support of approval of an abbreviated new drug application, or ANDA. The FDCA, FDA regulations, and other applicable regulations and policies provide incentives to manufacturers to create modified, non-infringing versions of a drug to facilitate the approval of an ANDA or other application for generic substitutes. These manufacturers might only be required to conduct a relatively inexpensive study to

show that their product has the same active ingredient(s), dosage form, strength, route of administration, conditions of use, and labeling as our product and that the generic product is bioequivalent to ours, meaning it is absorbed in the body at the same rate and to the same extent. These generic equivalents, which must meet the same quality standards as branded pharmaceuticals, would be significantly less costly than ours to bring to market, and companies that produce generic equivalents are generally able to offer their products at lower prices. Thus, after the introduction of a generic competitor, a significant percentage of the sales of any branded product is typically lost to the generic product. Accordingly, competition from a generic equivalent would materially adversely impact our ability to successfully commercialize our equivalent product.

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

The biopharmaceutical industries, particularly in the pain and OA market, are intensely competitive and subject to rapid and significant technological change. We have competitors worldwide, including major multinational pharmaceutical and biotechnology companies. For example, the injectable OA treatment market today includes many injectable immediate-release steroids, including TA, the active ingredient in ZILRETTA, as well as hyaluronic acid, or HA, injections. Injectable therapies, such as ZILRETTA, are used primarily after oral medications no longer provide adequate pain relief. To the extent that new or improved oral or other systemically administered pain medications are introduced that demonstrate better long-term efficacy and safety, patients and physicians may further delay the introduction of injectable therapies, including ZILRETTA, in the OA treatment continuum. ZILRETTA could also face competition from other formulations or devices that deliver pain medication on an extended basis, such as transdermal delivery systems or implantable devices.

Many of our competitors have substantially greater financial, technical, and other resources, such as larger research and development staffs and experienced commercial and manufacturing organizations. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. As a result, these companies may obtain regulatory approval more rapidly than we can and be more effective in selling and marketing their products. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring, or licensing on an exclusive basis drug products or drug delivery technologies that are more effective or less costly than our products or product candidates.

We believe that our ability to successfully compete will depend on, among other things:

- the efficacy and safety of our products and product candidates, including relative to third-party products and product candidates;
- the ability to distinguish safety and efficacy from existing, less expensive generic alternative therapies;
- the time it takes for our product candidates to complete clinical development and receive marketing approval;
- the ability to maintain a good relationship with regulatory authorities;
- the ability to commercialize and market our products that receive regulatory approval;
- the price of our products, including in comparison to branded or generic competitors;
- whether coverage and adequate levels of reimbursement are available under private and governmental health insurance plans, including Medicare;
- the ability to protect our intellectual property rights;
- the ability to manufacture on a cost-effective basis and sell commercial quantities of our products that receive regulatory approval; and
- acceptance of our products that receive regulatory approval by patients, physicians, and other healthcare providers.

If our competitors market products that are more effective, safer, less expensive, or reimbursed at higher rates than ours or offer discounts or rebates that allow physicians to receive more net revenue, we may not achieve commercial success. In addition, the biopharmaceutical industry is characterized by rapid technological change. Because we have limited research and development capabilities, it may be difficult for us to stay abreast of the rapid changes in each technology. If we fail to stay at the forefront of technological change, we may be unable to compete effectively.

If we are unable to maintain sales and marketing capabilities or enter into agreements with third parties to market, distribute, and sell our products, we may be unable to generate adequate revenue.

Our strategy is to commercialize ZILRETTA in the United States with a targeted sales and marketing organization. While we have established our commercial team and our sales force, we do not have prior experience commercializing pharmaceutical

products as an organization. In order to successfully market ZILRETTA, we must continue to build and maintain our sales, marketing, managerial, compliance, and related capabilities or make arrangements with third parties to perform these services. These efforts will continue to be expensive and time-consuming, and we compete with other pharmaceutical and biotechnology companies to recruit, hire, train, and retain marketing and sales personnel. If we are unable to maintain adequate sales, marketing, and distribution capabilities, whether independently or with third parties, we may not generate significant revenue from ZILRETTA.

Additionally, our strategy in the United States includes distributing ZILRETTA through a limited network of third parties. While we have entered into these agreements to purchase or distribute ZILRETTA in the United States, the counterparties may not perform as agreed or may terminate their agreements with us. For example, ZILRETTA sales are concentrated with certain specialty distributors, which together represented the vast majority of our sales for the past two years. Loss of any specialty distributor through contract termination or its failure to distribute effectively would adversely affect product distribution. While we have entered into these agreements on commercially reasonable terms, there is no guarantee that we will be able to continue to do so, if at all.

We and any third parties that we may engage in the future will be competing with many companies that currently have extensive and well-funded marketing and sales operations. If we, alone or with commercialization partners, are unable to compete successfully against these established companies, the commercial success of our approved products will be limited. In addition, if we are unable to effectively develop and maintain our commercial team, including our U.S. sales force, or maintain and, if needed, expand, our customer base, our ability to effectively commercialize our products and generate product revenues would be limited.

Customer buying patterns and other factors may cause our quarterly results to fluctuate, which may adversely affect our short-term results.

Our results of operations, and product revenues in particular, may vary from period to period due to a variety of factors, including the buying patterns of our direct purchasers, which vary from quarter to quarter and may be impacted by seasonality (such as in the first quarter of the year when patient deductibles tend to be reset). If our customers limit their product purchases, our sales could be adversely affected. Further, any changes in purchasing patterns or inventory levels, increases in product returns, delays in purchasing products, or delays in payment for products by our customers could also have a negative impact on our revenue and results of operations. In addition, we are unable to predict the long-term impact of COVID-19 and the pace of recovery and how this may impact purchases of ZILRETTA by healthcare providers in the future, as individual providers and their patients may have different responses as the pandemic evolves.

If we are unable to effectively train and equip our sales force, our ability to successfully commercialize ZILRETTA will be harmed.

We are required to expend significant time and resources to train our sales force to be credible, persuasive, and compliant with applicable laws in marketing ZILRETTA for its approved indication. In addition, we must train our sales force to ensure that an appropriate and compliant message about ZILRETTA is being delivered. Due to the COVID-19 pandemic, our MBMs have been using a mix of in-person and virtual interactions with physicians to convey key information about ZILRETTA and aid physicians and their staff in prescribing and obtaining reimbursement for ZILRETTA. While we have attempted to maintain the effectiveness of our sales and marketing efforts, it may not be as effective as in the pre-COVID environment, as access to some providers remains limited. If we are unable to maintain an effectively trained sales force and equip them with compliant and effective materials, including medical and sales literature to help them appropriately inform and educate customers regarding the potential benefits and safety of ZILRETTA and its proper administration, our efforts to successfully commercialize ZILRETTA could be jeopardized, which would negatively impact our ability to generate product revenues.

If we are unable to achieve and maintain adequate levels of third-party payer coverage and reimbursement for any product we may offer, on reasonable pricing terms, that product's commercial success may be severely hindered.

Successful sales of ZILRETTA and any other approved product candidates depend on the availability of coverage and adequate reimbursement from third-party payers, including governmental healthcare programs, such as Medicare and Medicaid, managed care organizations, and commercial payers, among others. Patients who are prescribed medicine for the treatment of their conditions generally rely on third-party payers to reimburse all or part of the costs associated with their prescription drugs. Coverage and adequate reimbursement from third-party payers are critical to product acceptance. Coverage decisions may depend upon clinical and economic standards that disfavor drug products when more established or lower cost therapeutic alternatives are already available or subsequently become available. The resulting reimbursement payment rates for ZILRETTA and, if approved, our product candidates, might not be adequate or may require co-payments that patients find unacceptably high.

In addition, the market for any product we may sell may depend significantly on access to third-party payers' medical policies, drug formularies, or lists of medications for which third-party payers provide coverage and reimbursement, as well as inclusion of that product on the reimbursement policies and formularies used by large physician practices and hospitals. The industry competition to be included in such policies or formularies often leads to downward pricing pressures on pharmaceutical companies, and we may be required to offer discounted rates to certain government and other payers to ensure coverage of our drugs. Also, third-party payers, physician practices, and hospitals may refuse to include a particular branded drug in their policies or formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or other alternative is available, or when the reimbursement landscape is unclear.

Governmental and commercial third-party payers are developing increasingly sophisticated methods of controlling healthcare costs. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement, and requirements for substitution of generic products. In addition, in the United States, no uniform policy of coverage and reimbursement for drug products exists among third-party payers. Therefore, coverage and reimbursement for drug products can differ significantly from payer to payer, and one payer's determination to provide coverage for a product does not ensure that other payers also will provide coverage. As a result, the coverage determination process is often a time-consuming and costly and will require us to provide scientific and clinical support for the use of our products to each payer separately, with no assurance that coverage and adequate reimbursement will be obtained.

Further, we believe that coverage and reimbursement will likely be increasingly restricted in many or all markets. Third-party coverage and reimbursement for any product we may sell in a particular market may not be available or adequate or may be more limited than the indications for which the drug is approved by other regulatory authorities. Moreover, eligibility for coverage and reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sales, and distribution costs. If coverage and reimbursement are not available or only available at limited levels for a product we may sell, we may not be able to successfully commercialize that product, which could have a material adverse effect on our business, results of operations, financial condition, and prospects.

Guidelines and recommendations published by various organizations can reduce the use of our products.

Government agencies promulgate regulations and guidelines directly applicable to us and to our products and product candidates. In addition, professional societies, practice management groups, private health and science foundations, and organizations involved in various diseases from time to time may also publish guidelines or recommendations to the healthcare and patient communities with respect to specific classes of products. Recommendations of government agencies or these other groups or organizations may relate to such matters as usage, dosage, route of administration, and use of concomitant therapies. Recommendations or guidelines that do not recognize a product, suggest limitations or inadequacies of a product, or suggest the use of competitive or alternative products as the standard of care to be followed by patients and healthcare providers could result in decreased use or adoption of any of our products.

ZILRETTA is available to a much larger number of patients and in broader populations through commercial sales as compared to the patients in our clinical studies, and the results of ZILRETTA's use in such larger context may be inconsistent with the results from our clinical studies.

While the FDA granted approval of ZILRETTA based on the data included in the NDA, we do not know whether the results that served as the basis for the FDA's approval of ZILRETTA will be consistent with commercial results as a large number of patients and broader populations are exposed to ZILRETTA and are exposed over longer periods of time, including results related to safety and efficacy. New data relating to ZILRETTA, including from adverse event reports or our ongoing studies of ZILRETTA in other indications, may result in additional changes to the product label and may adversely affect sales, or result in withdrawal of ZILRETTA from the market. The FDA and regulatory authorities in other jurisdictions may also consider any new data in connection with further marketing approval applications. If ZILRETTA or any additional approved products cause serious or unexpected side effects after receiving market approval, a number of potentially significant negative consequences could result, including withdrawal of product approval, restrictions on its distribution, additional labeling, changes in promotion or product administration, or a requirement for additional clinical studies. Any of these events could prevent us from maintaining market acceptance of the affected product and could substantially increase the costs of commercializing ZILRETTA or any additional products.

Recently enacted and future legislation, including health care reform measures, may increase the difficulty and cost for us to commercialize ZILRETTA and any future products and may affect the prices we may obtain.

The United States and some foreign jurisdictions are considering, or have enacted, a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell ZILRETTA and any other products approved for sale profitably. Among policy makers and third-party payers in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality, and expanding access. In the United States, the pharmaceutical industry has been a particular focus of

these efforts and has been, and may continue to be, significantly affected by major legislative, congressional, and enforcement initiatives. Moreover, in some foreign jurisdictions, pricing of prescription pharmaceuticals is already subject to government control.

For example, the Patient Protection and Affordable Care Act, as amended, or PPACA, was intended to, among other items, broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add transparency requirements for the healthcare and health insurance industries, impose taxes and fees on the health industry, and impose additional health policy reforms. Among the PPACA provisions of importance to the pharmaceutical industry are the imposition of additional fees, an increase in required rebates and a change in their method of calculation, discounts to eligible beneficiaries under Medicare Part D, expanded discount eligibility for entities under the Public Health Service pharmaceutical pricing program, expansion of the range of existing manufacturer liabilities, expanded eligibility for Medicaid programs, additional reporting requirements, expansion of and enhanced penalties under fraud and abuse laws, and improved market access for follow-on biologic products. There have been legal and political challenges to PPACA. For example, the United States Supreme Court is currently reviewing the constitutionality of the PPACA. It is unclear how the Supreme Court ruling, other such litigation, and the healthcare reform efforts of the Biden administration will impact PPACA and our business. We expect that PPACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and lower reimbursement, as well as additional downward pressure on the price that we receive for any approved product, including ZILRETTA. It is also possible that additional governmental action is taken in response to COVID-19.

Risks Related to Product Development and Regulatory Compliance

We may be unable to remove the LOU or expand the label for ZILRETTA and may never obtain regulatory approval of ZILRETTA for additional indications, approval of our other product candidates in the United States, or obtain approval for or commercialize ZILRETTA or our other product candidates outside of the United States, which would limit our ability to realize their full market potential.

The time required to obtain approval by the FDA and comparable foreign authorities is unpredictable but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions.

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

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

The lengthy approval process, as well as the unpredictability of future clinical trial results, may result in our failing to obtain regulatory approval to market ZILRETTA in additional indications or to market our other product candidates at all, which would harm our business, results of operations, and prospects.

In addition, any approval obtained may include fewer or more limited indications than we request, be contingent on the performance of costly post-marketing clinical trials or require a label that does not include the labeling claims necessary or desirable for successful commercialization of that product candidate. For example, while ZILRETTA has been approved for the management of OA pain of the knee, the approved product label originally contained a limitation of use, or LOU, stating that ZILRETTA is not intended for repeat administration. On December 26, 2019, the FDA approved our supplemental new drug application, or sNDA, to revise the product label for ZILRETTA. The sNDA was based on data from an open-label Phase 3b clinical trial, which indicated that repeat administration of ZILRETTA for treatment of OA knee pain was safe and

well tolerated with no deleterious impact on cartilage or joint structure observed through X-ray analysis. While the LOU was updated from stating ZILRETTA was not intended for repeat administration to stating that the efficacy and safety of repeat administration of ZILRETTA have not been demonstrated, the FDA did not find the data submitted in the sNDA sufficient to approve a removal of the LOU entirely. If we are unable to remove the LOU or expand the label for ZILRETTA, our ability to fully market ZILRETTA may be limited. Any of the foregoing could harm the commercial prospects for our product candidates.

Our product candidates may not receive regulatory approval despite success in clinical trials. Even if we successfully obtain regulatory approval to market one or more of our product candidates, our revenue will be dependent, to a significant extent, upon the size of the markets in the territories for which we gain regulatory approval. If the markets for patients or indications that we are targeting are not as significant as we estimate, we may not generate significant revenue from sales of such products, if approved.

Clinical development is a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results. Clinical failure can occur at any stage of clinical development.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of subsequent clinical trials. In particular, the results generated in our completed ZILRETTA pivotal Phase 3 clinical trial do not ensure that any future ZILRETTA clinical trial will be successful or consistent with the results generated in the Phase 3 trial.

Product candidates may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. For example, while FX201 has demonstrated successful results in numerous animal models, we cannot predict if it will prove to behave similarly in our on-going Phase 1 trial or subsequent trials. In addition to the safety and efficacy trials of any product candidate, clinical trial failures may result from a multitude of factors including flaws in trial design, dose selection, placebo effect, and patient enrollment criteria. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. In addition, data obtained from trials and studies are susceptible to varying interpretations, and regulators may not interpret our data as favorably as we do, which may delay, limit, or prevent regulatory approval. If any product candidate is found to be unsafe or lack efficacy or feasibility in particular indications, we will not be able to obtain regulatory approval for the indication and our business could be materially harmed.

Interim, topline, and preliminary data from our preclinical studies and clinical trials may change as more 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 disclose interim, topline, or preliminary data from our preclinical studies and clinical trials, which is based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change as more data become available. We may also announce topline data following the completion of a preclinical study or clinical trial, which may be 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 interim, topline, or preliminary 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, interim, topline, and preliminary data should be viewed with caution until the final data are available. Adverse differences between previous preliminary or interim data and future interim or final data could significantly harm our business prospects.

Interim data from clinical trials that we may complete are also 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, as higher doses or different dosing regimens are explored, or as patients from our clinical trials continue other treatments. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects. Further, disclosure of interim data by us, our collaboration partners, or our competitors could result in volatility in the price of our common stock.

In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine to be material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities, or otherwise regarding a particular product candidate or our business. If the interim, topline, or preliminary data that we report differ from future or more comprehensive data, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for and commercialize our product candidates, our business, operating results, prospects, or financial condition may be harmed.

COVID-19 will likely continue to have an adverse impact on our clinical trials and further development of our pipeline.

COVID-19's impact on the healthcare industry is significant and has impacted our on-going clinical trials and may disrupt further development of our pipeline. For example, in April 2020, we temporarily suspended the active Phase 1 clinical trial evaluating the safety and tolerability of FX201. The decision was made in consideration of guidance from the FDA to ensure the safety of trial participants and minimize risk to trial integrity from disruptions caused by COVID-19. In addition, we decided to terminate the Phase 2 trial evaluating the efficacy of ZILRETTA in patients with shoulder OA and adhesive capsulitis, given the small number of patients enrolled in the trial, the uncertainty as to when we would be able to restart the study, and the costs required to maintain it in an inactive status.

As COVID-19 continues to disrupt our ability to conduct clinical trials, we cannot predict with confidence when we will restart enrollment in or initiate new clinical trials for our clinical candidates in the United States and other countries. For example, while we subsequently restarted our Phase 1 clinical trial of FX201 in late May 2020, and we intend to initiate a trial investigating ZILRETTA in patients with shoulder OA and start clinical development of FX301 in 2021, we cannot guarantee that COVID-19's impact or restrictions implemented by government agencies or healthcare facilities in response to COVID-19 will not force us to delay, suspend, or terminate these trials, and we cannot predict how access to, utilization of, and efficacy of COVID-19 vaccines may influence such impacts and restrictions. These impacts of COVID-19 will increase the costs of completing clinical development and delay our ability to obtain marketing approval for our pipeline product candidates and ZILRETTA for additional indications.

Delays in clinical trials are common and have many causes, and any delay could result in increased costs to us and jeopardize or delay our ability to obtain regulatory approval for our product candidates.

We may experience delays in clinical trials of our products and product candidates. Our clinical trials may not begin on time, have an effective design, enroll a sufficient number of patients, or be completed on schedule, if at all. Our clinical trials can be delayed for a variety of reasons, including:

- inability to raise funding necessary to initiate or continue a trial;
- delays in obtaining regulatory approval to commence a trial;
- delays in reaching agreement with the FDA on final trial design;
- imposition of a clinical hold for safety reasons or following an inspection of our clinical trial operations or trial sites by the applicable regulatory authorities;
- delays in reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites;
- delays in obtaining required institutional review board approval at each site;
- delays in recruiting suitable patients to participate in a trial;
- delays in having patients complete participation in a trial or return for post-treatment follow-up;
- clinical sites dropping out of a trial to the detriment of enrollment;
- time required to add new clinical sites;
- delays by our contract manufacturers to produce and deliver sufficient supply of clinical trial materials; or
- the impact of COVID-19 and actions taken to mitigate its spread, including access to, utilization of, and timing of COVID-19 vaccines.

If initiation or completion of our clinical trials are delayed for any reason, our development costs may increase, our approval process could be delayed, and our ability to commercialize our product candidates could be materially harmed, which could have a material adverse effect on our business.

Changes in funding for the FDA and other government agencies or their ability to maintain operations due to the impact of COVID-19 or other reasons could hinder their ability to hire and retain key leadership and other personnel, prevent new products from being developed or commercialized in a timely manner, or otherwise prevent those agencies from performing normal functions on which our business operations rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels; ability to hire and retain key personnel and accept payment of user fees; the continuing impact of COVID-19; and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies may also slow their review and approval of new drugs, labeling supplements, and other regulatory requests to be acted upon, which would adversely affect our business.

The FDA granted marketing approval of ZILRETTA for the treatment of patients with OA pain of the knee, and we could face liability if a regulatory authority determines that we are promoting a product for any off-label uses.

A company may not promote "off-label" uses for its drug products. An off-label use is the use of a product for an indication that is not described in the product's FDA-approved label in the United States or for uses in other jurisdictions that differ from those approved by the applicable regulatory agencies. Physicians, on the other hand, may prescribe products for off-label uses. Although the FDA and other regulatory agencies do not regulate a physician's choice of drug treatment made in the physician's independent medical judgment, they do restrict promotional communications from pharmaceutical companies or their employees with respect to off-label uses. A significant number of pharmaceutical companies have been the target of inquiries and investigations at the U.S. federal and state levels in connection with the promotion of products for unapproved uses and other sales practices, including pricing and Medicare of Medicaid reimbursement violations. A company that is found to have promoted off-label use of its product may be subject to significant liability, including substantial civil and criminal fines, damage awards, and other sanctions, such as consent decrees and corporate integrity agreements pursuant to which its activities would be subject to ongoing scrutiny and monitoring. Any regulatory enforcement action, *qui tam* suit by a private individual, or resulting fines, awards, or other sanctions would have an adverse effect on our revenue, business, financial prospects, and reputation.

We intend to comply with all promotional requirements, but we cannot be sure that regulatory agencies will agree that we have not violated those requirements. For example, we may communicate certain results from our clinical trials that are consistent with, but not directly included in, a product label. While we believe that our communication of these data is in accordance with FDA guidance and applicable laws, we cannot be certain that the FDA or other regulatory agencies will agree with our use of these data, and our sales force may use such data in a way that is inconsistent with our policies. As a result, we may be subject to significant liabilities, and our management's attention could be diverted to handle any such alleged violations.

Any relationships with healthcare professionals, principal investigators, consultants, actual and potential customers, and third-party payers in connection with our current and future business activities are and will continue to be subject to federal and state healthcare laws. If we do not comply, or only partially comply, with such laws, we could face criminal sanctions, civil penalties, administrative penalties, imprisonment, exclusion, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements and oversight, and curtailment or restructuring of our operations.

Our operations are directly or indirectly subject to various federal and state healthcare laws, such as fraud and abuse laws, anti-kickback laws, false claims laws, marketing expenditure tracking and disclosure (or "sunshine") laws, government price reporting, and health information privacy and security laws. Our costs associated with compliance and exposure to potential liability under these laws are likely to increase with increased commercialization. These laws may impact, among other things, our activities with investigators and research subjects, as well as sales, marketing, promotion, manufacturing, distribution, pricing, discounting, customer incentive programs, physician speaker programs, and other business arrangements and activities. We may also be subject to patient privacy regulation in the jurisdictions in which we conduct our business.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations may involve substantial costs. It is possible that governmental and enforcement authorities will conclude that our business practices, including activities undertaken by third parties on our behalf, may not comply with statutes, regulations, or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any applicable laws or regulations, we may be subject to significant penalties, including damages, fines, disgorgement, imprisonment, possible exclusion from participation in government healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements and oversight, and curtailment or restructuring of our operations. If a government authority were to conclude that we provided improper advice or encouraged the submission of a false claim for reimbursement, we could face governmental action against us. If any of the above occurs, it could adversely affect our ability to operate our business and our results of operations. Additionally, if any providers or entities with whom we expect to do business are found not to be in compliance with applicable laws, they may be subject to significant sanctions, including exclusion from government-funded healthcare programs.

ZILRETTA is still subject to substantial ongoing regulatory requirements, and our product candidates may face future development and regulatory difficulties.

The FDA approved ZILRETTA only for the treatment of OA knee pain. If any additional clinical studies of ZILRETTA are negative, the FDA could decide to withdraw approval, add warnings, or narrow the approved indication in the product label.

ZILRETTA is, and, if approved, our other product candidates, will also be, subject to ongoing FDA requirements governing the labeling, packaging, storage, distribution, safety surveillance, advertising, promotion, record-keeping, and reporting of

safety and other post-market information. The holder of an approved NDA is obligated to monitor and report adverse events, or AEs, and any failure of a product to meet the specifications in the NDA. The holder of an approved NDA must also submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling, or manufacturing process. Advertising and promotional materials must comply with FDA rules and are subject to FDA review, in addition to other potentially applicable federal and state laws.

In addition, manufacturers of drug products and their facilities are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with current good manufacturing practices, or cGMP, and adherence to commitments made in the NDA. If we or a regulatory agency discover previously unknown problems with a product, such as AEs of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions relative to that product or the manufacturing facility, including requiring recall or withdrawal of the product from the market or suspension of manufacturing.

We rely on third-party collaborators to assist us in meeting our reporting and related obligations. While we work closely with these third parties, we do not control all of their activities. If our third-party collaborators do not meet the relevant commitments, we may fail to meet our applicable regulatory requirements.

If we fail to comply with applicable regulatory requirements for any product we may sell, a regulatory agency may take a variety of actions, including seeking an injunction, imposing penalties, withdrawing approval, or seizing the product. Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize our products and generate revenue.

If we fail to develop, acquire, or in-license other potential future product candidates or products, our business and prospects will be limited.

Our long-term growth strategy is to develop, acquire, or in-license and commercialize a portfolio of potential future product candidates. Our primary means of expanding our pipeline of product candidates is to select and acquire or in-license product candidates for the treatment of therapeutic indications that complement or augment our current pipeline, or that otherwise fit into our development or strategic plans on terms that are acceptable to us, or develop improved formulations and delivery methods for existing products. Developing new formulations or delivery methods of existing or potential future product candidates or identifying, selecting, and acquiring or in-licensing promising product candidates requires substantial technical, financial, and human resources expertise. Efforts to do so may not result in the actual development, acquisition, or in-license of a particular product candidate, potentially resulting in a diversion of our management's time and the expenditure of our resources with no resulting benefit. If we are unable to add additional product candidates to our pipeline, our long-term business and prospects will be limited.

Risks Related to Our Reliance on Third Parties

We rely completely on third parties to manufacture our commercial supplies of ZILRETTA and our preclinical and clinical drug supplies for our product candidates.

If we were to experience an unexpected loss of supply of any product or product candidate for any reason, we could experience disruptions in commercial supply or delays, suspensions, or terminations of clinical trials or regulatory submissions. We do not currently have nor do we plan to acquire the infrastructure or capability internally to manufacture our preclinical and clinical drug supplies, and we lack the resources and the capability to manufacture any of our product candidates on a clinical or commercial scale. The facilities used by our contract manufacturers or other third-party manufacturers to manufacture our products and product candidates must obtain and maintain approval by the FDA. While we work closely with our third-party manufacturers on the manufacturing process for our products and product candidates, including quality audits, we generally do not control the implementation of the manufacturing process of, and are completely dependent on, our contract manufacturers or other third-party manufacturers for compliance with cGMP regulatory requirements and for manufacture of both active drug substances and finished drug products. If our contract or other third-party manufacturers cannot successfully manufacture material that conforms to applicable specifications and the strict regulatory requirements in place, they will not be able to secure or maintain regulatory approval for their manufacturing facilities.

In addition, we have no control over the ability of our contract manufacturers or other third-party manufacturers to maintain adequate quality control, quality assurance, and qualified personnel. If an applicable regulatory authority does not approve, or withdraws approval for, these facilities for the manufacture of our products and product candidates, we may need to find alternative manufacturing facilities, which would significantly impact our ability to commercialize, develop, or obtain or maintain regulatory approval for our products and product candidates.

We are particularly reliant on Patheon with respect to maintaining ZILRETTA manufacturing capacity. Patheon facilities required approval from the FDA as a condition of regulatory approval for ZILRETTA, and. because Patheon manufactures ZILRETTA in the United Kingdom, or U.K., it needs to maintain and update its facility license with the applicable U.K. regulatory agencies, and any delay or inability to do so would delay or prevent Patheon from being able to produce commercial supplies of ZILRETTA. Furthermore, the manufacturing process for ZILRETTA is unique and involves specialized equipment and proprietary processes, which increases the risk that Patheon will experience manufacturing delays.

We also rely on our manufacturers to purchase from third-party suppliers the materials necessary to produce ZILRETTA and our product candidates. There are a limited number of suppliers for these materials, and we may need to assess alternate suppliers to prevent a possible disruption in production. We do not have any control over the process or timing of the acquisition of these raw materials. Moreover, we currently do not have any agreements for the commercial production of these raw materials. Although we generally do not begin a clinical trial unless we believe we have a sufficient supply of a product candidate to complete the clinical trial, any significant delay in the supply of a product candidate, or the raw material components thereof, for an ongoing clinical trial due to the need to replace a contract manufacturer or other third-party manufacturer could considerably delay completion of our clinical trials, product testing, and potential regulatory approval of our product candidates. If our manufacturers or we are unable to purchase these raw materials, there would be a shortage in supply, which would impair our ability to generate revenue from the sale of our products.

We expect to continue to depend on contract manufacturers or other third-party manufacturers for the foreseeable future. We have entered into long-term commercial supply agreements with our current contract manufacturers in order to maintain adequate supplies to manufacture finished ZILRETTA drug product. We may, however, be unable to enter into such agreements or do so on commercially reasonable terms for potential future product candidates, which could have a material adverse impact upon our business.

We rely on sole sources of supply for our products and product candidates, and any supply chain disruption may limit our product sales or cause delay in developing, obtaining approval for, and commercializing our product candidates.

Currently, we use the following sole sources of supply for manufacturing ZILRETTA: Farmabios SpA for TA, Evonik Corporation for PLGA, and Patheon for finished microsphere drug product. Because of the unique equipment and process for loading TA onto PLGA microspheres, transferring finished drug product manufacturing activities for ZILRETTA to an alternate supplier would be a time-consuming and costly endeavor, and there are only a limited number of manufacturers that we believe are capable of performing this function for us. Switching finished drug suppliers may involve substantial cost and could result in a failure to maintain adequate product supplies. We expect that for the foreseeable future Patheon will be the only manufacturer qualified as a commercial supplier of ZILRETTA with the FDA. From time to time, commercial batches of ZILRETTA may fail to meet required specifications and be unavailable for commercial sale. If we experience multiple successive batch failures, or if supply from Patheon is otherwise interrupted, there could be a significant disruption in commercial supply. Any alternative vendor would need to be qualified through an NDA supplement, which could result in further delay. Applicable regulatory agencies may also require additional studies if a new ZILRETTA supplier is relied upon for commercial production.

As the global impact of COVID-19 continues, we may experience additional disruptions that could severely impact our supply chain, which would disrupt our clinical trials and commercialization efforts. To the extent that our vendors are unable to comply with their obligations under our agreements with them or cannot deliver or are delayed in delivering goods and services to us, our ability to continue meeting commercial demand for our products or advancing development of our product candidates may become impaired. We cannot be certain that we will be able to maintain sufficient commercial supply if there is a rapid increase in ZILRETTA demand as the impact of COVID-19 abates.

These factors could cause the disruption of the commercialization of ZILRETTA; delay clinical trials, regulatory submissions, required approvals, or commercialization of any of our other product or product candidates; cause us to incur higher costs; or prevent us from commercializing them successfully. Furthermore, if our suppliers fail to deliver the required clinical or commercial quantities of active pharmaceutical ingredient on a timely basis and at commercially reasonable prices and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical trials may be delayed or we could lose potential revenue in the event of a product stockout for ZILRETTA or any of our other product candidates that is approved and launched.

Our other product candidates also rely on sole sources of supply for the preclinical and clinical supply of materials. The manufacturing processes for our product candidates are complex, and it may be difficult or impossible to finalize appropriate processes for the scaled manufacture of the product candidates.

Manufacturing issues may arise that could increase product and regulatory approval costs or disrupt or delay commercialization.

As we scale up manufacturing of ZILRETTA and other product candidates, we may encounter product, packaging, equipment, and process-related issues that may require refinement or resolution in order to proceed with our planned clinical trials or maintain regulatory approval for commercial marketing. In the future, we may identify impurities or other product related issues, which could result in increased scrutiny by regulatory authorities, suspensions of commercial activities or product recalls, delays in our clinical program and regulatory approval, increases in our operating expenses, or failure to obtain or maintain approval for our products or product candidates.

We rely on third parties to conduct our preclinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed.

We rely upon and plan to continue to rely upon third-party CROs to monitor and manage data for our preclinical and clinical programs. We rely on these parties for execution of our preclinical studies and clinical trials and control only certain aspects of their activities. Nevertheless, we are 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 are required to comply with FDA laws and regulations regarding current good clinical practice, or GCP, which are also required by comparable foreign regulatory authorities for all of our products in clinical development. Regulatory authorities enforce GCP through periodic inspections of trial sponsors, principal investigators, and trial sites. If we or any of our CROs fail to comply with applicable GCP, the clinical data generated in our clinical trials may be deemed unreliable and the applicable regulatory authority may require us to perform additional clinical trials before approving our marketing applications. We cannot be certain that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP regulations. In addition, our clinical trials must be conducted with product produced under cGMP regulations. While we have agreements governing activities of our CROs, we have limited influence over their actual performance. In addition, portions of the clinical trials for our product candidates may be conducted outside of the United States, which will make it more difficult for us to monitor CROs and perform visits of our clinical trial sites and will force us to rely heavily on CROs to ensure the proper and timely conduct of our clinical trials and compliance with applicable regulations.

Some of our CROs have an ability to terminate their respective agreements with us for patient safety reasons or concerns regarding our financial stability. If any of our relationships with these third-party CROs terminate, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms. In addition, our CROs are not our employees, and, except for remedies available to us under our agreements with such CROs, we cannot control whether or not they devote sufficient time and resources to our preclinical and clinical programs. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements, or for other reasons, our clinical trials may be extended, delayed, or terminated, and we may not be able to obtain regulatory approval for or successfully commercialize our product candidates. Consequently, our results of operations and the commercial prospects for our product candidates would be harmed, our costs could increase substantially, and our ability to generate revenue could be delayed significantly.

Switching or adding CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition, and prospects.

We may not be successful in establishing effective collaborations or maintaining development and commercialization collaborations, and our partners may not devote sufficient resources to the development or commercialization of our products or product candidates or may otherwise fail in development or commercialization efforts, which could adversely affect our ability to develop or commercialize certain of our products or product candidates and our financial condition and operating results.

We may seek third-party collaborators or licensees for the development and commercialization of our product candidates. For instance, we have entered into an exclusive license agreement for the development and commercialization of ZILRETTA in China, Hong Kong, Macau and Taiwan with HK Tainuo and Jiangsu Tainuo. We intend to seek to enter into additional collaborations for developing, marketing and commercializing our product candidates in certain territories at the appropriate time in the future. We have, with respect to our collaboration with HK Tainuo and Jiangsu Tainuo, and will likely have, with respect to any additional collaboration arrangements with any third parties, limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to

generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements and otherwise to comply with their contractual obligations.

Any of our existing or future collaborations may not ultimately be successful, which could have a negative impact on our business, results of operations, financial condition and growth prospects. In addition, the terms of any such collaboration or other arrangement may not prove to be favorable to us or may not be perceived as favorable, which may negatively impact the trading price of our common stock. In some cases, we may be responsible for continuing development of a product or product candidate or research program under collaboration and the payment we receive from our partner may be insufficient to cover the cost of this development. Moreover, collaborations and sales and marketing arrangements are complex and time consuming to negotiate, document and implement and they may require substantial resources to maintain.

Conflicts may arise between us and partners, such as conflicts concerning the interpretation of clinical data, the achievement of milestones, the division of development or commercialization responsibilities or expenses, the interpretation of financial provisions, or the ownership of intellectual property developed during the collaboration. If any such conflicts arise, a partner could act in its own self-interest, which may be adverse to our best interests. Any such disagreement between us and a partner could delay or prevent the development or commercialization of our products or product candidates, and in turn prevent us from generating sufficient revenue to achieve or maintain profitability:

Further, we are subject to the following additional risks associated with our current and any future collaborations with third parties, the occurrence of which could cause our collaboration arrangements to fail:

- collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may fail in their development or commercialization efforts with our product candidate, in which event the development and commercialization of such product candidate could be delayed or terminated;
- collaborators may delay clinical trials, insufficiently fund a clinical trial program, stop a clinical trial, abandon a product candidate, repeat or conduct new clinical trials, or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- collaborators may fail to successfully design or implement clinical trials and may collect and publish clinical trial data that are inconsistent with, or contradictory to, our clinical trial results;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation;
- collaborators may deviate from established guidelines, instructions, or best practices for product handling and storage, which may compromise the safety, purity, potency, and effectiveness of our products and potentially result in the occurrence of serious adverse events in patients using our products;
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates;
- reductions in the payments we believe are due to us pursuant to the applicable collaboration arrangement;
- actions taken by a partner inside or outside our collaboration that could negatively impact our rights or benefits under our collaboration; or
- partner unwillingness to keep us informed regarding the progress of its development and commercialization activities or to permit public disclosure of the results of those activities.

Risks Related to Our Business Operations and Industry

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

We are highly dependent on the members of our executive team, the loss of whose services could adversely impact the achievement of our objectives. While we have entered into employment agreements or offer letters with each of our executive officers, any of them could leave our employment at any time, as all of our employees are “at will” employees. Recruiting and retaining other qualified employees for our business, including scientific and technical personnel, will also be critical to our success. There is currently a shortage of skilled executives and other technically qualified personnel in our industry,

particularly in the greater Boston, Massachusetts, area where our headquarters is located, which is likely to continue. As a result, competition for skilled personnel is intense, and the turnover rate can be high. We may not be able to attract and retain personnel on acceptable terms given the competition among numerous biotechnology and pharmaceutical companies for individuals with similar skill sets. In addition, failure in the commercialization of ZILRETTA or clinical studies of our product candidates may make it more challenging to recruit and retain qualified personnel. The inability to recruit or the loss of the services of any executive or key employee might impede the progress of our development and commercialization objectives.

We face potential product liability, and, if successful claims are brought against us, we may incur substantial liability.

The use of our product candidates in clinical trials and the sale of our products expose us to the risk of product liability claims. Product liability claims might be brought against us by consumers, healthcare providers, or others coming into contact with our products or product candidates. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- impairment of our business reputation and perception of our products in the market;
- withdrawal or suspension of marketing approvals;
- withdrawal of clinical trial participants;
- costs due to related litigation;
- distraction of management's attention from our primary business;
- substantial monetary awards to patients or other claimants;
- the inability to commercialize our product candidates;
- decreased demand for our products approved for commercial sale; and
- reputational harm.

Our current product liability insurance coverage may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive, and in the future we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. On occasion, large judgments have been awarded in class action or mass tort lawsuits based on drugs that had unanticipated adverse effects. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business.

Collaborations with third parties to develop and commercialize products outside of the United States subject us to a variety of risks associated with international operations that could materially and adversely affect our business.

Agreements with third parties to market ZILRETTA, and, if approved, our product candidates, outside of the United States, subject us to additional risks related to entering into international business relationships, including:

- different regulatory requirements for drug approvals in foreign countries;
- reduced protection for intellectual property rights;
- unexpected changes in tariffs, trade barriers, and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration, and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenue;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- different government payer systems, multiple payer-reimbursement regimes or patient self-pay systems, and price controls;
- potential noncompliance with the FCPA, the U.K. Bribery Act 2010, or similar antibribery and anticorruption laws in other jurisdictions as well as various regulations pertaining to data privacy, such as the GDPR;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters.

If we fail to comply with applicable U.S. and foreign privacy and data protection laws and regulations, we may be subject to liabilities that adversely affect our business, operations, and financial performance.

We are subject to laws and regulations requiring that we take measures to protect the privacy and security of certain information we gather and use in our business. For example, HIPAA, as amended, and its implementing regulations impose certain regulatory and contractual requirements regarding the privacy and security of personal health information on covered entities, such as health plans, healthcare clearinghouses, and certain healthcare providers and their business associates and covered subcontractors that perform certain services involving the use or disclosure of personal health information. In addition, numerous other federal and state laws, such as state security breach notification laws, state health information privacy laws, and federal and state consumer protection laws, govern the collection, use, and storage of personal information.

We may also be subject to or affected by foreign laws and regulation governing the collection, use, disclosure, security, transfer, and storage of personal data, such as information that we collect about employees, patients, and healthcare providers in connection with clinical trials and our other operations. The global legislative and regulatory landscape for privacy and data protection continues to evolve, and implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future. This evolution may create uncertainty in our business, result in liability, or impose additional costs on us. The cost of compliance with these laws, regulations, and standards is high and is likely to increase in the future. It is possible that each of these privacy laws may be interpreted and applied in a manner that is inconsistent with our practices. Any failure or perceived failure by us to comply with laws, regulations, or standards could result in negative publicity, diversion of management time and effort, and proceedings against us by governmental entities or others. In many jurisdictions, enforcement actions and consequences for noncompliance are rising. As we continue to expand into other foreign countries and jurisdictions, we may be subject to additional laws and regulations that may affect how we conduct business.

Business interruptions could delay us in the process of developing or commercializing our products and product candidates.

We are vulnerable to natural disasters and other events that could disrupt our operations. We do not carry insurance for natural disasters and may not carry sufficient business interruption insurance to compensate us for losses that may occur. Further, our operations, and those of our contractors, consultants, and collaborators, could be subject to various natural or man-made disasters or business interruptions, which could have a material adverse effect on our business operations. To the extent our suppliers and service providers are unable to comply with their obligations under our agreements with them or cannot deliver or are delayed in delivering goods and services to us, our ability to continue meeting commercial demand for our products or advancing development of our product candidates may become impaired.

Exposure to U.K. political developments could impact our suppliers and harm our business.

The U.K.'s referendum to leave the EU, or "Brexit," has caused and may continue to cause disruptions to capital and currency markets worldwide. The full impact of the Brexit decision, however, remains to be seen. Our results of operations and access to capital may be negatively affected by interest rate, exchange rate, and other market and economic volatility, as well as regulatory and political changes. The tax consequences of the U.K.'s withdrawal from the EU are uncertain as well. Brexit may also have a detrimental effect on our suppliers, which could, in turn, adversely affect our revenues and financial condition.

Risks Related to Our Intellectual Property

If we are unable to obtain or protect intellectual property rights, we may not be able to compete effectively in our market.

We rely upon a combination of patents, trade secret protection, confidentiality agreements, and proprietary know how and intend to seek marketing exclusivity for any approved product in order to protect the intellectual property related to our products and product candidates. To date we have three issued patents covering ZILRETTA in the United States.

The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. As a result, the issuance, scope, validity, enforceability, and commercial value of our patent rights and our current or future licensors' or collaborators' patent rights are highly uncertain. The patent applications that we own or in-license may fail to result in issued patents with claims that cover our products or product candidates in applicable countries. Even for our issued and future patents, third parties may challenge their inventorship, ownership, validity, enforceability, or scope in the courts or issuing patent offices. This may result in such patents being narrowed or invalidated, which could limit our ability to stop others from using or commercializing similar or identical technologies or products or limit the duration of the patent protection for our technologies and products. If this were to occur, early generic competition could be expected against the covered product and potentially reduce the value of our product candidates in development. Also, a third party may challenge our rights to patents and patent applications that we license from third parties. Furthermore, even if they are

unchallenged, our patents and patent applications may not adequately protect our intellectual property or prevent others from designing around our claims.

If our patent applications with respect to any product or product candidate fail to issue or if their breadth or strength of protection is threatened, it could dissuade companies from collaborating with us in development and threaten our ability to commercialize any resulting products. We cannot offer any assurances about which, if any, patents will issue or whether any issued patents will not be found invalid and unenforceable or will go unthreatened by third parties. Further, if we encounter delays in regulatory approvals for additional indications or in additional jurisdictions, the period of time during which we could market ZILRETTA or any product candidate under patent protection could be reduced. See “Business—Patents and Patent Applications” in this Annual Report on Form 10-K for additional information regarding our material patents and patent applications.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable, processes for which patents are difficult to enforce, and any other elements of our drug development process that involve proprietary know-how, information, or technology that is not covered by patents. For example, we maintain trade secrets with respect to certain of the formulation and manufacturing techniques related to the TA-formulated PLGA microspheres in ZILRETTA, including those that relate to precise pharmaceutical release. Although we generally require all of our employees to assign their inventions to us, and all of our employees and third parties who have access to our proprietary know-how, information, or technology to enter into confidentiality agreements, we cannot provide any assurances that all such agreements have been duly executed or that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Further, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent material disclosure of the non-patented intellectual property related to our technologies to third parties, and there is no guarantee that we will have any such enforceable trade secret protection, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations, and financial condition.

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

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. There is a substantial amount of litigation involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions, and inter party reexamination proceedings before the U.S. Patent and Trademark Office, or U.S. PTO. Numerous U.S. and foreign issued patents and pending patent applications owned by third parties exist in the fields in which we and our collaborators are commercializing or developing product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our products and product candidates may be subject to claims of infringement of the patent rights of third parties.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture, or methods for treatment related to the use or manufacture of our products or product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our products or product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our products or product candidates, any drug substance formed during the manufacturing process, or any final product itself, the holders of such patents may be able to block our ability to commercialize such product or product candidate unless we obtain a license under the applicable patents, or until such patents expire. Similarly, if any third-party patent were held by a court of competent jurisdiction to cover aspects of our formulations or methods of use, the holders of any such patent may be able to block our ability to develop and commercialize the applicable product or product candidate unless we obtain a license or until such patent expires. In either case, such a license may not be available on commercially reasonable terms or at all.

Parties making claims against us may request injunctive or other equitable relief, which relief could effectively block our ability to further develop and commercialize one or more of our products or product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys’ fees for willful infringement, obtain one or more licenses from third parties, pay royalties, or redesign our infringing products or manufacturing processes, which may be impossible or require substantial time and monetary expenditure. We cannot predict whether any such license would be available at all or whether

it would be available on commercially reasonable terms. Furthermore, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research, manufacture clinical trial supplies, or allow commercialization of our product candidates. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all, and would then be unable to further develop and commercialize one or more of our products or product candidates, which could harm our business significantly. We cannot provide any assurances that third-party patents do not exist that might be enforced against our products, resulting in either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties or other forms of compensation to third parties.

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

Competitors may infringe our issued patents, licensed patents, or our other intellectual property. In some cases, it may be difficult or impossible to detect third-party infringement or misappropriation of our intellectual property rights, even in relation to issued patent claims, and proving any such infringement may be even more difficult. Accordingly, for such undetectable infringement or misappropriation our ability to recover damages will be negligible, and we could be at a market disadvantage because we may lack the resources of some of our competitors to monitor for and detect infringement. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents. In addition, in any patent infringement proceeding, a court may decide that a patent of ours is invalid or unenforceable, in whole or in part; construe the patent's claims narrowly; or refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology. An adverse result in litigation proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly. 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.

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

Periodic maintenance fees on any issued patent are due to be paid to patent agencies in several stages over the lifetime of the patent. In addition, patent agencies require compliance with a number of procedural, documentary, fee payment, and other provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. If we fail to maintain the patents and patent applications covering our product candidates, our competitors might be able to enter the market, which would have a material adverse effect on our business.

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

Filing, prosecuting, and defending patents on all of our product candidates throughout the world would be prohibitively expensive, and the laws of foreign countries may not protect our rights to the same extent as United States law. Consequently, we may not be able to prevent third parties from infringing on our intellectual property rights in all countries outside the United States, and competitors may use our technologies in jurisdictions where we have not obtained patent protection and may export otherwise infringing products to territories where we have patent protection but enforcement is not as strong as in the United States.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business.

Our owned or licensed patents directed to our product candidates may expire or have limited commercial life before the product candidate is approved for marketing in a relevant jurisdiction.

Given the amount of time required for the development, testing, and regulatory review of product candidates, patents protecting our product candidates might expire before or shortly after those candidates obtain regulatory approval, which may subject us to increased competition and reduce or eliminate our ability to recover our development costs. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. Although we may be able to seek extensions of patent terms where available, we cannot be certain that an extension will be granted, or, if granted, what the applicable time period or the scope of patent protection afforded during any extended period will be. The applicable authorities in each country may not agree with our assessment of

whether such extensions are available and may refuse to grant extensions to our patents or grant more limited extensions than we request. If this occurs, our competitors may take advantage of our investment in development and trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.

Our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology industry involve both technological and legal complexity and is therefore costly, time-consuming, and inherently uncertain. In addition, in recent years the United States enacted patent reform legislation and U.S. Supreme Court rulings narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty regarding our ability to obtain patents in the future, this combination has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts, and the U.S. PTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

We have in-licensed or acquired a portion of our intellectual property necessary to develop our product candidates, and, if we fail to comply with our obligations under any of these arrangements, we could lose such intellectual property rights.

We rely on several arrangements with third parties that give us rights to intellectual property necessary for the manufacture of ZILRETTA and the development of FX201 and FX301. Our current arrangements impose various development, royalty, and other obligations on us. If we materially breach these obligations, or if our counterparts fail to adequately perform their respective obligations, these exclusive arrangements could be terminated, which would result in our inability to develop, manufacture, and sell products that are covered by such intellectual property.

We may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates, and we have done so from time to time. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. If so, we may be required to expend significant time and resources to develop or license replacement technology. If we are unable to do so, we may be unable to develop or commercialize our affected product candidates, which could harm our business significantly. We cannot provide any assurances that third-party patents do not exist that might be enforced against our current product candidates or future products, resulting in either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties or other forms of compensation to such third parties.

In many cases, patent prosecution of our licensed technology is controlled solely by the licensor. If our licensors fail to obtain and maintain patent or other protection for the proprietary intellectual property we license from them, we could lose our rights to the intellectual property or our exclusivity with respect to those rights, and our competitors could market competing products using the intellectual property. In certain cases, we control the prosecution and maintenance of patents resulting from licensed technology. If we breach any of those obligations, we may incur significant liability to our licensing partners. Licensing of intellectual property is of critical importance to our business and involves complex legal, business, and scientific issues and is complicated by the rapid pace of scientific discovery in our industry. Disputes may arise regarding intellectual property subject to a licensing agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor not covered by the licensing agreement;
- the sublicensing of patent and other rights under our collaborative development relationships;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our partners; and
- the priority of invention of patented technology.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

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

We rely on our trademarks and trade names to build name recognition among potential partners and potential customers in our markets of interest. If we are unable to successfully register our trademarks and trade names and establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively, and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks or trade names may be ineffective and could result in substantial costs and diversion of resources and could adversely impact our financial condition or results of operations. In addition, our unregistered trademarks or trade names may be challenged, infringed, circumvented, or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names. Competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our unregistered trademarks or trade names. If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

Risks Related to Ownership of Our Common Stock

The market price of our common stock may be highly volatile, you may not be able to resell your shares at a desired market price, and you could lose all or part of your investment.

The trading price of our common stock is likely to be volatile due to a variety of factors, including the following:

- success or perceived success of the commercialization of ZILRETTA;
- the impact and duration of COVID-19 and actions taken to mitigate its spread;
- inability to obtain approval for additional indications for ZILRETTA;
- failure to successfully develop and commercialize additional product candidates;
- changes in the structure of healthcare payment systems;
- adverse results or delays in clinical trials;
- inability to obtain additional funding;
- changes in laws or regulations applicable to our products or product candidates;
- inability to obtain adequate supply for our products or product candidates, or the inability to do so at acceptable prices;
- adverse regulatory decisions;
- introduction of new products or technologies by our competitors;
- failure to meet or exceed product development or financial projections we provide to the public;
- failure to meet or exceed the estimates and projections of the investment community;
- the perception of the pharmaceutical industry by the public, legislatures, regulators, and the investment community;
- announcements of significant acquisitions, strategic partnerships, joint ventures, or capital commitments by us or our competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters, and our ability to obtain patent protection for our technologies;
- additions or departures of key scientific or management personnel;
- significant lawsuits, including patent, product liability, or stockholder litigation;
- changes in the market valuations of similar companies;
- sales of our common stock by us or our stockholders in the future; and
- trading volume of our common stock.

The trading price of our common stock may also be dependent upon the valuations and recommendations of the analysts who cover our company. If our results do not meet these analysts' forecasts, the expectations of our investors, or any financial guidance or expectations we provide to investors, the market price of our common stock could decline. Our ability to meet analysts' forecasts (including revenue and profitability), investors' expectations, and our own guidance or financial expectations is substantially dependent on our ability to increase sales of ZILRETTA and to successfully commercialize ZILRETTA in the United States. Because we have not yet fully commercialized ZILRETTA, we and the analysts who cover

our company have limited ability to accurately predict future sales results, and actual results may differ materially from expectations.

In addition, the stock market in general, and the Nasdaq Global Market in particular, have experienced extreme price and volume fluctuations, and we have in the past experienced volatility that has been unrelated or disproportionate to our operating performance. Broad market and industry factors may continue to negatively affect the market price of our common stock, regardless of our operating performance.

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

As a public company, we incur significant legal, accounting, and other expenses and devote a substantial amount of time in complying with a variety of laws, regulations, and rules, such as the Securities Exchange Act of 1934, as amended; the Sarbanes-Oxley Act; the Dodd-Frank Wall Street Reform and Consumer Protection Act; and the rules of the Nasdaq Global Market. We also incur costs indirectly resulting from those laws, regulations, and rules. For example, they have made it more difficult and more expensive for us to obtain director and officer liability insurance, and we may be required to incur substantial costs to maintain our current levels of such coverage. In addition, stockholder activism and the current political environment may lead to new regulations and disclosure obligations involving additional costs and further impacting how we operate our business.

If the estimates we make, or the assumptions on which we rely, in preparing our consolidated financial statements prove inaccurate, our actual results may vary from those reflected in our projections and accruals.

Our consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of our assets, liabilities, revenues, and expenses; the amounts of charges accrued by us; and the related disclosure of contingent assets and liabilities. On an ongoing basis, our management evaluates our critical and other significant estimates and judgments, including, among others, those associated with revenue recognition and accrued expenses related to preclinical and clinical development costs. We base our estimates on historical experience, known trends and events, contractual milestones, and various other factors that we believe to be reasonable under the circumstances. Actual results may differ from these estimates under different assumptions or conditions. Any significant differences between our actual results and our estimates could materially affect our financial position, results of operations, and cash flows.

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

Sales of a substantial number of shares of our common stock in the public market, or the perception that these sales might occur, could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity or convertible debt securities. We cannot predict the effect that sales may have on the prevailing market price of our common stock.

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

We may need significant additional capital in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell such equity securities in one or more transactions at prices, under terms, and in a manner as we may determine from time to time. These sales may result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders.

Pursuant to our 2013 equity incentive plan, we are authorized to grant stock options and other equity-based awards to our employees, directors, and consultants. The number of shares available for future grant under this plan automatically increases each year by 4% of all shares of our capital stock outstanding as of December 31 of the prior calendar year, subject to the ability of our board of directors to reduce the size of any such increase. Currently, we plan to register the increased number of shares available for issuance under this plan each year. If our board of directors elects to increase the number of shares available for future grant by a significant amount each year, our stockholders would experience additional dilution, which could cause our stock price to fall.

We are at risk of securities class action litigation.

Securities class action litigation has often been brought against a company following a decline in the market price of its securities, and pharmaceutical companies have experienced significant stock price volatility in recent years. If we face such

litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

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

Our net operating loss ("NOL") carryforwards could expire unused and be unavailable to offset future tax liabilities because of their limited duration or because of restrictions under U.S. tax law, which only permits NOLs generated in tax years ending on or before December 31, 2017, to be carried forward for twenty years. Our federal NOLs generated in tax years ending after December 31, 2017, may be carried forward indefinitely, but the deductibility of federal NOLs, particularly for tax years beginning after December 31, 2020, may be limited. It is uncertain if and to what extent various states will conform to the Tax Act and the CARES Act.

Section 382 of the Internal Revenue Code of 1986, as amended, contains rules that limit the ability of a company that undergoes an ownership change to utilize its NOLs and tax credits existing as of the date of such ownership change. Under the rules, such an ownership change is generally any change in ownership of more than 50% of a company's stock within a rolling three-year period. The rules generally focus on changes in ownership among stockholders considered by the rules as owning, directly or indirectly, 5% or more of the stock of a company or in connection with new issuances of stock by the company. Future ownership changes may further limit the amount of NOL carryforwards we could use to offset future taxable income.

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

We have never declared or paid any cash dividend on our common stock. We currently anticipate that we will retain future earnings for the development, operation, and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Additionally, our loan agreements with certain banks contain covenants that restrict our ability to pay dividends. Any return to stockholders will therefore be limited to the appreciation of their stock.

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

Some provisions of our charter documents and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders, and may prevent attempts by our stockholders to replace or remove our current management. These provisions include:

- authorizing the issuance of "blank check" preferred stock, the terms of which may be established and shares of which may be issued without stockholder approval;
- limiting the removal of directors by the stockholders;
- creating a staggered board of directors;
- requiring all stockholder actions to be taken at a meeting of our stockholders;
- eliminating the ability of stockholders to call a special meeting of stockholders; and
- establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings.

These provisions may frustrate or prevent any attempts by our stockholders to replace or remove members of management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing such members. In addition, we are subject to Section 203 of the Delaware General Corporation Law, which generally prohibits a Delaware corporation from engaging in any of a broad range of business combinations with an interested stockholder for a period of three years following the date on which the stockholder became an interested stockholder, unless such transactions are approved by our board of directors. This provision could delay or prevent a change of control, even if desired by or beneficial to our stockholders. Further, other provisions of Delaware law may also discourage, delay, or prevent someone from acquiring us or merging with us.

General Risk Factors

We rely significantly on information technology and any failure, inadequacy, interruption, or security lapse of that technology, including any cybersecurity incidents, could harm our ability to operate our business effectively.

Despite the implementation of security measures, our internal computer systems and those of third parties with which we contract are vulnerable to cyber-attacks, computer viruses, unauthorized access, physical damage, and telecommunication and

electrical failures. System failures, accidents, or security breaches could cause interruptions in our operations and could result in a material disruption of our commercial and clinical activities and business operations, in addition to possibly requiring substantial expenditures of resources to remedy. The loss of clinical trial data could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our development programs or the development of our product candidates could be delayed, and trade secrets or other competitive advantages could be lost.

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

We employ individuals who were previously employed at other biotechnology or pharmaceutical companies and may be subject to claims that we or our employees, consultants, or independent contractors have used or disclosed confidential information of third parties. We may also be subject to claims that former employers or other third parties have an ownership interest in our patents. Litigation may be necessary to defend against these claims. There is no guarantee of success in defending these claims, and, even if we are successful, litigation could result in substantial cost and be a distraction to our management and other employees.

If we fail to maintain an effective system of internal controls over financial reporting, we may not be able to accurately report our financial results or prevent fraud, which could cause stockholders to lose confidence in our public reporting and harm our business and the trading price of our common stock.

Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation, could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with the Sarbanes-Oxley Act, or by our independent registered public accounting firm, may reveal deficiencies in such internal controls that are deemed to be material weaknesses or that require prospective or retroactive changes to our controls, procedures, or consolidated financial statements, which could result in substantial additional costs. Inadequate internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our common stock.

Item 1B. Unresolved Staff Comments

Not applicable.

Item 2. Properties

Our principal facilities consist of office and laboratory space. We lease approximately 42,000 square feet of office space in Burlington, Massachusetts under a lease that expires in April 2025. In addition, we lease approximately 5,300 square feet of laboratory space in Woburn, Massachusetts, under a lease that expires in 2022.

Item 3. Legal Proceedings

We are not currently a party to any material legal proceedings.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

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

Market Information

Our common stock is listed on the Nasdaq Global Market and trades under the symbol "FLXN".

Holders of Record

As of March 1, 2021, there were approximately 15 stockholders of record of our common stock. Certain shares are held in "street" name and accordingly, the number of beneficial owners of such shares is not known or included in the foregoing number.

Securities Authorized for Issuance under Equity Compensation Plans

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

Recent Sales of Unregistered Securities

There were no unregistered sales of equity securities by us during the year ended December 31, 2020.

Issuer Repurchases of Equity Securities

None.

Item 6. Selected Financial Disclosure

None.

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

The following discussion and analysis of financial condition and results of operations should be read in conjunction with "Item 6. Selected Financial Data" and our consolidated financial statements and related notes appearing elsewhere in this Annual Report. This discussion and analysis and other parts of this Annual Report contain forward-looking statements based upon current beliefs, plans and expectations that involve risks, uncertainties and assumptions, such as statements regarding our plans, objectives, expectations, intentions and projections. Our actual results and the timing of selected events could differ materially from those anticipated in these forward-looking statements as a result of several factors, including those set forth under "Item 1A. Risk Factors". You should carefully read the "Risk Factors" section of this Annual Report to gain an understanding of the important factors that could cause actual results to differ materially from our forward-looking statements. Please also see the section entitled "Special Note Regarding Forward-Looking Statements."

Overview

We are a biopharmaceutical company focused on the discovery, development and commercialization of novel, local therapies for the treatment of patients with musculoskeletal conditions, beginning with osteoarthritis, the most common form of arthritis, referred to as OA.

On October 6, 2017, the U.S. Food and Drug Administration, or FDA, approved our product, ZILRETTA, for marketing in the United States. ZILRETTA is the first and only extended-release, intra-articular, or IA (meaning in the joint), injection indicated for the management of OA related knee pain. ZILRETTA is a non-opioid therapy that employs our proprietary microsphere technology to provide extended pain relief. The pivotal Phase 3 trial, on which the approval of ZILRETTA was based, showed that ZILRETTA met the primary endpoint of pain reduction at Week 12, with statistically significant pain relief extending through Week 16.

We have two pipeline programs focused on the local treatment of musculoskeletal conditions: FX201, which is an investigational IA gene therapy product candidate in clinical development for the treatment of OA, and FX301, an investigational NaV1.7 inhibitor product candidate, which is being developed as a locally administered peripheral analgesic nerve block for management of post-operative pain.

We were incorporated in Delaware in November 2007, and to date we have devoted substantially all of our resources to developing our product candidates, including conducting clinical trials with our product candidates, preparing for and undertaking the commercialization of ZILRETTA, providing general and administrative support for these operations and protecting our intellectual property. From our inception through December 31, 2020, we have raised approximately $913 million and funded our operations primarily through the sale of our common stock, convertible preferred stock, and convertible debt, as well as debt financing. Until such time, if ever, as we can generate sufficient product revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings, government or third-party funding, and licensing or collaboration arrangements.

We have incurred net losses in each year since our inception in 2007. Our net losses were $113.7 million, $149.8 million, and $169.7 million for the years ended December 31, 2020, 2019, and 2018, respectively. As of December 31, 2020, we had an accumulated deficit of $782.3 million. Substantially all of our net losses resulted from costs incurred in connection with our development programs and from selling, general and administrative expenses associated with our operations.

We anticipate that we will incur losses over the next few years. We expect that our operating expenses will continue to increase in connection with our ongoing activities, as we:

- continue the development and commercialization of ZILRETTA, including our on-going and future clinical trials;
- continue to scale-up manufacturing activities including the supply of clinical trial materials and commercial batches;
- maintain a sales and marketing infrastructure for the commercialization of ZILRETTA;
- expand our development activities and advance FX201 and FX301;
- maintain, expand and protect our intellectual property portfolio; and
- add operational, financial and management information systems and personnel, including personnel to support our product development and commercialization efforts and operations.

ZILRETTA is a physician-administered product, and therefore physicians are required to purchase and manage the inventory of ZILRETTA, prior to administering the product to patients. Physicians obtain reimbursement for ZILRETTA from the applicable third-party payer, such as Medicare or a health insurance company, only after it has been administered to patients. This is called a "buy and bill" process. Because physicians are at financial risk for the cost of a "buy and bill" product until they have been reimbursed, concerns about reimbursement can impact a physician's decision to use the product. We received the product-specific J code (J3304) for ZILRETTA from CMS on January 1, 2019. We believe that the product-specific J

code provides prescribers with confidence in the reimbursement of ZILRETTA, as product-specific J codes are universally recognized by Medicare, as well as by commercial payers.

Our promotional and marketing activities have increased since launch, as our field sales representatives, known as Musculoskeletal Business Managers, or MBMs, have expanded prescriber awareness and utilization of ZILRETTA. Furthermore, our Field Access Managers have been working with physician practices to navigate any reimbursement challenges and to support their awareness of the product-specific J code for reimbursement of ZILRETTA.

We closely track and provide updates on several uptake metrics to provide perspective on the progress of the ZILRETTA launch. Since the launch in November 2017 through December 31, 2020:

- 4,248 accounts had purchased ZILRETTA, reflecting growth of 176 new purchasing accounts compared to September 30, 2020, when 4,072 accounts had purchased product.
- 78% of purchasing accounts (3,321) had placed at least one reorder, up from 3,153 accounts that had reordered ZILRETTA as of September 30, 2020
- 1,242 accounts had made ZILRETTA purchases of more than 50 units; 1,170 accounts had purchased between 11 and 50 units; and 1,836 accounts had purchased between 1 and 10 units
- Accounts that had purchased more than 50 ZILRETTA units accounted for 307,988 of the total 345,697 ZILRETTA units purchased.

Impact of the Coronavirus Global Pandemic

On March 11, 2020, the World Health Organization made the assessment that a novel strain of coronavirus, which causes the COVID-19 disease, had become a global pandemic (“COVID-19”). COVID-19 has presented a substantial public health and economic challenge around the world and is affecting our employees, patients, communities and business operations, as well as the U.S. economy and financial markets. COVID-19 continues to rapidly evolve. In mid-March, the U.S. declared a national emergency and states implemented various “social distancing” and “stay at home” measures to mitigate the spread of COVID-19. In turn, we closed our offices in Burlington, MA, and instructed all of our employees to work from home, including all of our field-based personnel. We also undertook prudent and disciplined steps to reduce expenses across the organization, including hiring and travel freezes, elimination of live presence at medical and industry conferences, reductions in in-person physician speaker programs, reductions in select marketing programs and materials, and elimination of non-essential operating expenses. In addition, we paused our Phase 1 trial of FX201, discontinued our Phase 2 trial investigating ZILRETTA in shoulder OA and adhesive capsulitis (AC) due to the small number of patients enrolled at the time and temporarily paused manufacturing activities for ZILRETTA to avoid excess levels of inventory.

Due to the significant impacts of COVID-19 on patient flow at healthcare providers, purchases of ZILRETTA by healthcare providers dropped precipitously in the latter part of March and that decline continued into early April. Despite this precipitous decline, our MBMs found most accounts were receptive to “e-detailing,” and in the second quarter our MBMs were able to gain access to some healthcare providers who had been previously very difficult to reach due to busy office and surgical schedules. Additionally, by the end of the second quarter, the vast majority of our MBMs were able to return to the field to conduct in-person calls on accessible physician offices. Correspondingly, our Commercial team conducted a series of focus groups with physicians around the country who confirmed that the pandemic had resulted in many patients facing extensive delays for total knee replacement (TKR) surgery and caused other patients to postpone surgery indefinitely.

In the second half of 2020, we began to see ZILRETTA sales that were more in line with our pre-COVID-19 expectations, and we believe that our ZILRETTA sales performance in the second half of the year was driven by several key factors: a normalization of office visits despite the presence of COVID-19; the continued tailwind from delays and deferrals in total knee arthroplasties; deeper penetration in existing healthcare provider accounts that purchase ZILRETTA; and the addition of new ZILRETTA purchasing accounts. We believe that as more and more clinicians gain more experience with ZILRETTA, it will come to be recognized as a best-in-class treatment option for patients with knee OA. While we are encouraged by the growth of ZILRETTA purchases by healthcare providers we saw in the second half of 2020, the future impact of COVID-19and access to, utilization of, and efficacy of COVID-19 vaccines on our business remains uncertain and unpredictable.

Financial Overview

Revenue

Product Revenue

Net product sales consist of sales of ZILRETTA, which was approved by the FDA on October 6, 2017, and launched in the United States shortly thereafter. We had not generated any revenue prior to the launch of ZILRETTA.

License Revenue

On March 30, 2020, we entered into an exclusive license agreement with HK Tainuo and Jiangsu Tainuo, a subsidiary of China Shijiazhuang Pharmaceutical Co, Ltd. for the development and commercialization (other than manufacturing) of ZILRETTA in Greater China (consisting of mainland China, Hong Kong and Macau, and Taiwan). Under the terms of the agreement, HK Tainuo paid us an upfront payment of $10.0 million, of which $5.0 million was received as of June 30, 2020, and the remaining $5.0 million was received as of September 30, 2020. We are also eligible to receive up to $32.5 million in aggregate development, regulatory and commercial sales milestone payments. All payments received from HK Tainuo are subject to the applicable Hong Kong withholding taxes. HK Tainuo is responsible for the clinical development, product registration and commercialization of ZILRETTA in Greater China and Jiangsu Tainuo serves as the guarantor of HK Tainuo's obligations and responsibilities under the agreement. We are solely responsible for the manufacture and supply of ZILRETTA to HK Tainuo for all clinical and commercial activities. The terms related to product manufacturing and supply, including pricing and minimum purchase requirements agreed to in the license agreement, will be covered by a separate supply agreement. All amounts owed to us are nonrefundable and non-creditable once paid. We concluded that the license and supply obligations were not distinct performance obligations, and therefore the transaction price will be recognized as revenue as our supply obligation is fulfilled over the term of the supply agreement, which has not yet commenced. No revenue was recognized associated with this contract as of December 31, 2020.

Cost of Sales

Cost of sales consists of third-party manufacturing costs, freight and indirect overhead costs associated with sales of ZILRETTA. Cost of sales also includes period costs related to certain inventory manufacturing services, inventory adjustment charges, and unabsorbed manufacturing and overhead costs, as well as any write-offs of inventory that fails to meet specification or is otherwise no longer suitable for commercial manufacture. Based on our policy to expense costs associated with the manufacture of our products prior to regulatory approval, the majority of product sold during the year ended December 31, 2018, was manufactured and previously charged to research and development expense prior to FDA approval of ZILRETTA and therefore is not included in cost of sales during the period. As of December 31, 2018, all of the finished goods inventory that was previously expensed had been sold to customers.

From April to November 2020, as a result of COVID-19, we voluntarily, temporarily suspended manufacturing at Patheon. During this time, we continued to incur certain fixed overhead costs related to the operation of the manufacturing facility at Patheon while production activities were suspended. These fixed overhead costs would typically be capitalized to ZILRETTA inventory but were recorded to cost of sales over the period in which production was suspended.

Research and Development Expenses

Our research and development activities include: preclinical studies, clinical trials, and chemistry, manufacturing, and controls, or CMC activities. Our research and development expenses consist primarily of:

- expenses incurred under agreements with consultants, contract research organizations, or CROs, and investigative sites that conduct our preclinical studies and clinical trials;
- costs of acquiring, developing and manufacturing clinical trial materials;
- personnel costs, including salaries, benefits, stock-based compensation and travel expenses for employees engaged in scientific research and development functions;
- costs related to compliance with certain regulatory requirements;
- expenses related to the in-license of certain technologies; and
- allocated expenses for rent and maintenance of facilities, insurance and other general overhead.

We expense research and development costs as incurred. Our direct research and development expenses consist primarily of external-based costs, such as fees paid to investigators, consultants, investigative sites, CROs and companies that manufacture our clinical trial materials and potential future commercial supplies and are tracked on a program-by-program basis. We do not allocate personnel costs, facilities or other indirect expenses to specific research and development programs. These indirect expenses are included within the amounts designated as "Personnel and other costs" in the Results of Operations section below. Inventory acquired prior to receipt of the marketing approval of a product candidate is recorded as research and development expense as incurred.

Our research and development expenses decreased in 2020 relative to the prior year. As part of our expense reduction steps taken in response to the COVID-19 pandemic, we terminated the Phase 2 clinical trial investigating ZILRETTA in shoulder OA and AC and temporarily suspended the FX201 single ascending dose trial which resulted in a deferral of spending related to clinical trials, and eliminated other non-essential operating expenses. While the duration of COVID-19 and its impact on our ability to conduct clinical development are highly uncertain, we expect that a return to normal operations will likely result

in an increase in future research and development expenses. Specifically, our costs will increase as we conduct additional clinical trials for ZILRETTA and conduct further developmental activities for our pipeline programs, including our on-going Phase 1 trial of FX201 and our planned Phase 1b trial of FX301.

We cannot determine with certainty the duration of and completion costs associated with ongoing and future clinical trials or the associated regulatory approval process, post-marketing development of ZILRETTA or development of any product candidates in our pipeline. The duration, costs and timing associated with the further development of ZILRETTA or the development of other product candidates will depend on a variety of factors, including uncertainties associated with the results of our clinical trials. As a result of these uncertainties, we are currently unable to estimate with any precision our future research and development expenses for expanded indications for ZILRETTA or any product candidates in our pipeline.

Selling, General and Administrative Expenses

Selling, general and administrative expenses consist primarily of personnel costs, including salaries, related benefits, travel expenses and stock-based compensation of our executive, finance, business development, commercial, information technology, legal and human resources functions. Other selling, general and administrative expenses include an allocation of facility-related costs, patent filing expenses, and professional fees for legal, consulting, auditing and tax services.

Our selling, general and administrative expenses decreased in 2020 as compared to the prior year. As a result of the adverse effect of COVID-19 on our revenues, we took steps to reduce our operating expenses, including by reducing certain sales and marketing expenses through the elimination of live presence at medical and industry conferences, reductions in in-person physician speaker programs and reductions in select marketing programs and materials. We cannot determine with certainty the duration and timing of COVID-19, but we expect that a return to normal operations will likely result in an increase in future selling, general, and administrative expenses. In particular, we expect to incur ongoing increases in selling, general and administrative expenses related to the continued development and commercialization of ZILRETTA or any other product candidates, including external marketing expenses and the operation of our field sales force.

Other Income (Expense)

Interest income.

Interest income consists of interest earned on our cash and cash equivalents balances and our marketable securities. The primary objective of our investment policy is capital preservation.

Interest expense.

Interest expense consists of contractual interest on our 2024 Convertible Notes, which accrue interest at a rate of 3.375% per annum, payable semi-annually, our former term loan facility, which accrued interest at a fixed rate of 6.25% per annum, our term loan facility, which accrues interest at a floating interest rate equal to the greater of the Prime Rate (as reported in the Wall Street Journal) plus 1.50%, or 6.50% per annum, and our revolving credit facility, which accrues interest at a floating interest rate equal to the greater of the Prime Rate (as reported in the Wall Street Journal) or 5.50% per annum. Also included in interest expense is the amortization of the final payment on the term loan and the debt discount related to the convertible notes, which is being amortized to interest expense using the effective interest method over the expected life of the debt.

Other income (expense).

Other income (expense) consists of the net amortization or accretion of premiums and discounts related to our marketable securities, and our realized gains (losses) on redemptions of our marketable securities. We will continue to record either income or expense related to accretion of discounts or amortization of premiums on marketable securities for as long as we hold these investments. Also included in other income (expense) is the amortization of debt issuance costs on our term loan facility and the 2024 Convertible Notes, which are being amortized over the respective terms of the loans.

Income Taxes

As of December 31, 2020, we had $448.2 million and $340.1 million of federal and state net operating loss carryforwards, respectively, and $12.2 million and $5.2 million of federal and state research and development tax credit carryforwards, respectively, available to offset our future taxable income, if any. These federal net operating loss carryforwards and research and development tax credit carryforwards expire at various dates beginning in 2029, if not utilized and are subject to review and possible adjustment by the Internal Revenue Service. Approximately $258.7 million of the federal net operating losses have an indefinite carryforward. The state net operating loss carryforwards and research and development tax credit carryforwards expire at various dates beginning in 2030 and 2025, respectively, if not utilized and are subject to review and possible adjustment by the state tax authorities. At December 31, 2020, a full valuation allowance was recorded against our net operating loss carryforwards and our research and development tax credit carryforwards.

If we experience a greater than 50% aggregate change in ownership of certain stockholders over a three-year period, utilization of our then-existing net operating loss carryforwards and research and development tax credit carryforwards will be subject to an annual limitation.

As of December 31, 2020, the provision for income taxes consists of foreign withholding taxes related to our license agreement with HK Tainuo.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which we have prepared in accordance with generally accepted accounting principles in the United States, or GAAP. The preparation of our financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of our financial statements, and the reported revenue and expenses during the reported periods. We evaluate these estimates and judgments, including those described below, on an ongoing basis. We base our estimates on historical experience, known trends and events, contractual milestones and 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.

While our significant accounting policies are more fully described in Note 3 to our consolidated financial statements appearing elsewhere in this Form 10-K, we believe that the estimates and assumptions involved in the following accounting policies may have the greatest potential impact on our financial statements and, therefore, consider these to be critical for fully understanding and evaluating our financial condition and results of operations.

Revenue Recognition

We recognize revenue in accordance with Accounting Standards Codification ("ASC") Topic 606 - Revenue from Contracts with Customers ("Topic 606"). Under Topic 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to be entitled to in exchange for those goods or services.

To determine revenue recognition for arrangements that an entity determines are within the scope of Topic 606, the entity performs the following five steps: (i) identify the contract(s) with a customer, (ii) identify the performance obligations in the contract, (iii) determine the transaction price, (iv) allocate the transaction price to the performance obligations in the contract, and (v) recognize revenue when (or as) the entity satisfies a performance obligation. We only apply the five-step model to arrangements that meet the definition of a contract with a customer under Topic 606, including when it is probable that the entity will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of Topic 606, we assess the goods or services promised within each contract, determine those that are performance obligations, and assess whether each promised good or service is distinct. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

Product Revenue, Net— We primarily sell ZILRETTA to specialty distributors and a specialty pharmacy, who then subsequently resell ZILRETTA to physicians, clinics and certain medical centers or hospitals. We also contract directly with healthcare providers and intermediaries such as Group Purchasing Organizations ("GPOs"). In addition, we enter into arrangements with government payers that provide for government mandated rebates and chargebacks with respect to the purchase of ZILRETTA.

We recognize revenue on product sales when the customer obtains control of ZILRETTA, which occurs at a point in time (upon delivery to the customer). We have determined that the delivery of ZILRETTA to our customers constitutes a single performance obligation. There are no other promises to deliver goods or services beyond what is specified in each accepted customer order. Management has assessed the existence of a significant financing component in the agreements with our customers. The trade payment terms with our customers do not exceed one year and therefore management has elected to apply the practical expedient and no amount of consideration has been allocated as a financing component. Product revenues are recorded net of applicable reserves for variable consideration, including discounts and allowances.

Transaction Price, including Variable Consideration— Revenues from product sales are recorded at the net sales price (transaction price), which includes estimates of variable consideration for which reserves are established. Components of variable consideration include trade discounts and allowances, product returns, government chargebacks, discounts and rebates, and other incentives, such as voluntary patient assistance, and other fee for service amounts that are detailed within our contracts with our customers relating to the sale of ZILRETTA. These reserves, as detailed below, are based on the amounts earned, or to be claimed on the related sales, and are classified as reductions of accounts receivable (if the amount is payable to the customer) or a current liability (if the amount is payable to a party other than a customer). These estimates take

into consideration a range of possible outcomes which are probability-weighted in accordance with the expected value method in Topic 606 for relevant factors such as current contractual and statutory requirements, specific known market events and trends, industry data, and forecasted customer buying and payment patterns. Overall, these reserves reflect our best estimates of the amount of consideration to which we are entitled based on the terms of the respective underlying contracts.

The amount of variable consideration which is included in the transaction price may be constrained and is included in the net sales price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized under the contract will not occur in a future period. Actual amounts of consideration ultimately received may differ from our estimates. If actual results in the future vary from our original estimates, we will adjust these estimates, which would affect net product revenue and earnings in the period such variances become known.

Service Fees and Allowances—We compensate our customers and GPOs for sales order management, data, and distribution services. However, we have determined such services received to date are not distinct from our sale of products to the customer and, therefore, these payments have been recorded as a reduction of revenue within the statement of operations and comprehensive loss through December 31, 2020, as well as a reduction to trade receivables, net on the consolidated balance sheets.

Product Returns— Consistent with industry practice, we generally offer our customers a limited right of return for product that has been purchased from us based on the product's expiration date. We estimate the amount of our product sales that may be returned by our customers and record this estimate as a reduction of revenue in the period the related product revenue is recognized, as well as within accrued expenses and other current liabilities, net on the consolidated balance sheets. We currently estimate product return liabilities using available industry data and our own sales information, including our visibility into the inventory remaining in the distribution channel. We have received an immaterial amount of returns to date and we believe that returns of ZILRETTA will be minimal.

Chargebacks— Chargebacks for fees and discounts to qualified government healthcare providers represent the estimated obligations resulting from contractual commitments to sell products to qualified VA hospitals and 340b entities at prices lower than the list prices charged to customers who directly purchase the product from us. The 340b Drug Discount Program is a U.S. federal government program created in 1992 that requires drug manufacturers to provide outpatient drugs to eligible healthcare organizations and covered entities at significantly reduced prices. Customers charge us for the difference between what they pay for the product and the statutory selling price to the qualified government entity. These reserves are established in the same period that the related revenue is recognized, resulting in a reduction of product revenue and trade receivables, net. Chargeback amounts are generally determined at the time of resale to the qualified government healthcare provider by customers, and we generally issue credits for such amounts within a few weeks of the customer's notification to us of the resale. Reserves for chargebacks consist of credits that we expect to issue for units that remain in the distribution channel inventories at each reporting period-end that we expect will be sold to qualified healthcare providers, and chargebacks that customers have claimed, but for which we have not yet issued a credit.

Government Rebates— We are subject to discount obligations under state Medicaid programs and Medicare. These reserves are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability which is included in accrued expenses and other current liabilities on the consolidated balance sheets. For Medicare, we also estimate the number of patients in the prescription drug coverage gap for whom we will owe an additional liability under the Medicare Part D program. We anticipate our exposure to utilization from the Medicare Part D coverage gap discount program to be immaterial. For Medicaid programs, we estimate the portion of sales attributed to Medicaid patients and record a liability for the rebates to be paid to the respective state Medicaid programs. Our liability for these rebates consists of invoices received for claims from prior quarters that have not been paid or for which an invoice has not yet been received, estimates of claims for the current quarter, and estimated future claims that will be made for product that has been recognized as revenue, but which remains in the distribution channel inventories at the end of each reporting period.

Purchaser/Provider Discounts and Rebates—Beginning in the third quarter of 2019, we began offering rebates to eligible purchasers and healthcare providers that are variable based on volume of product purchased. Rebates are based on actual purchase levels during the rebate purchase period. We estimate these rebates and record such estimates in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability.

Other Incentives— Other incentives which we offer include voluntary patient assistance programs, such as the co-pay assistance program, which are intended to provide financial assistance to qualified commercially-insured patients with prescription drug co-payments required by payers. The calculation of the accrual for co-pay assistance is based on an estimate of claims and the cost per claim that we expect to receive associated with product that has been recognized as revenue but remains in the distribution channel inventories at the end of each reporting period. The adjustments are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current

liability which is included as a component of accrued expenses and other current liabilities on the consolidated balance sheets.

To date, our only source of product revenue has been from the U.S. sales of ZILRETTA, which we began shipping to customers in October 2017.

The following table summarizes activity in each of the product revenue allowance and reserve categories for the years ended December 31, 2020, 2019, and 2018:

(In thousands)	Service Fees, Allowances and Chargebacks	Government Rebates and Other Incentives	Product Returns	Purchaser/Provider Discounts and Rebates	Total
Balance as of December 31, 2017	$ 60	$ 15	$ 2	—	$ 77
Provision related to sales in the current year	1,688	502	124	—	2,314
Credit or payments made during the period	(1,147)	(26)	(1)	—	(1,174)
Balance as of December 31, 2018	601	491	125	—	1,217
Provision related to sales in the current year	5,527	261	334	2,685	8,807
Credit or payments made during the period	(4,281)	(375)	(57)	(1,029)	(5,742)
Adjustments related to prior period sales	—	(129)	—	—	(129)
Balance as of December 31, 2019	1,847	248	402	1,656	4,153
Provision related to sales in the current year	7,660	1,090	499	4,633	13,882
Credit or payments made during the period	(7,774)	(903)	(139)	(4,457)	(13,273)
Adjustments related to prior period sales	—	95	(134)	—	(39)
Balance as of December 31, 2020	$ 1,733	$ 530	$ 628	$ 1,832	$ 4,723

Research and Development Expenses

As part of the process of preparing our financial statements, we are required to estimate our accrued expenses. This process involves reviewing open contracts and purchase orders, communicating with applicable internal and vendor personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. Examples of estimated accrued research and development expenses include fees paid to:

- CROs in connection with clinical studies;
- investigative sites in connection with clinical studies;
- vendors related to product manufacturing, development and distribution of clinical supplies; and
- vendors in connection with preclinical development activities.

We record expenses related to clinical studies and manufacturing development activities based on our estimates of the services received and efforts expended pursuant to contracts with multiple CROs and manufacturing vendors that conduct and manage these activities on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract, and may result in uneven payment flows.

We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us. If timelines or contracts are modified based upon changes in the clinical trial protocol or scope of work to be performed, we modify our estimates of accrued expenses accordingly on a prospective basis. If we do not identify costs that we have begun to incur, or if we underestimate or overestimate the level of services performed or the costs of these services, our actual expenses could differ from our estimates. To date, we have not adjusted our estimates at any particular balance sheet date in any material amount.

RESULTS OF OPERATIONS

Year Ended December 31, 2020, Compared to Year Ended December 31, 2019

The following table summarizes our results of operations for the years ended December 31, 2020 and 2019. For a discussion of our results of operations for the year ended December 31, 2019, compared to the year ended December 31, 2018, see "Management's Discussion and Analysis of Financial Condition and Results of Operations" in our Annual Report on Form 10-K for the year ended December 31, 2019.

	Year Ended December 31,			
(In thousands)	**2020**	**2019**	**$ Change**	**% Change**
Revenues				
Product revenue, net	$ 85,552	$ 72,957	$ 12,595	17.3%
Operating expenses				
Cost of sales	19,249	9,960	9,289	93.3%
Research and development	54,326	69,559	(15,233)	(21.9)%
Selling, general and administrative	104,996	129,709	(24,713)	(19.1)%
Total operating expenses	178,571	209,228	(30,657)	(14.7)%
Loss from operations	(93,019)	(136,271)	43,252	(31.7)%
Other (expense) income				
Interest income	876	3,212	(2,336)	(72.7)%
Interest expense	(20,027)	(17,066)	(2,961)	17.4%
Other (expense) income	(1,041)	352	(1,393)	395.7%
Total other (expense) income	(20,192)	(13,502)	(6,690)	49.5%
Loss before income taxes	(113,211)	(149,773)	36,562	(24.4)%
Income tax expense	495	—	495	NM
Net loss	$ (113,706)	$ (149,773)	$ 36,067	(24.1)%

Product Revenue

For the years ended December 31, 2020 and 2019, we recorded $85.6 million and $73.0 million, respectively, of net product revenue. The year-over-year increase was due to an increase in the number of ZILRETTA units sold, which resulted in an increase in net revenue of $15.3 million, offset in part by a decrease of $3.3 million which was attributable to a decrease in the net price per unit primarily due to provider rebate offerings and other discounts. Included in net product revenue for the year ended December 31, 2020, were buy-ins by two of our specialty distributors for which the distributors received a modest discount. Those buy-ins accounted for approximately 4% of our total ZILRETTA units sold in 2020. We are unable to predict the long-term impact of COVID-19 and the pace of recovery and how this may impact purchases of ZILRETTA by healthcare providers, as individual providers and their patients have had different responses to the pandemic. For further discussion regarding our revenue recognition policy, see Note 3 to our consolidated financial statements appearing elsewhere in this Annual Report.

Cost of Sales

Cost of sales was $19.2 million and $10.0 million for the years ended December 31, 2020 and 2019, respectively. For the years ended December 31, 2020 and 2019, cost of sales consisted of $7.7 million and $8.4 million, respectively, related to the actual cost of units sold, $8.1 million and $0.9 million, respectively, as a result of unabsorbed manufacturing and overhead costs related to the operation of the facility at Patheon, and $1.0 million and $0.7 million, respectively, of period costs and other adjustments. Additionally, for the year ended December 31, 2020, cost of product sales included a charge resulting from the write-down of short-dated inventory of $2.5 million. There was no such charge for the year ended December 31, 2019.

Throughout much of 2020, while manufacturing was paused due to the impact of COVID-19, we continued to incur certain fixed overhead costs related to the operation of the manufacturing facility at Patheon which were recognized in our cost of sales. As a result, our cost of sales for the year ended December 31, 2020, was greater than what we have reported in periods prior to those impacted by COVID-19. We believe our cost of sales will become more normalized once ZILRETTA manufacturing has returned to pre-COVID-19 levels, and although manufacturing restarted in the fourth quarter of 2020, the full effects on our cost of sales will not be realized until 2021.

Research and Development Expenses

(In thousands)	Year Ended December 31, 2020	2019	$ Change	% Change
Direct research and development expenses by program:				
ZILRETTA	$ 9,635	$ 22,847	$ (13,212)	(57.8)%
FX201	7,082	$ 5,608	$ 1,474	26.3%
Portfolio expansion	5,580	5,776	(196)	(3.4)%
Other	1,821	3,120	(1,299)	(41.6)%
Total direct research and development expenses	24,118	37,351	(13,233)	(35.4)%
Personnel and other costs	30,208	32,208	(2,000)	(6.2)%
Total research and development expenses	$ 54,326	$ 69,559	$ (15,233)	(21.9)%

Research and development expenses were $54.3 million and $69.6 million for the years ended December 31, 2020 and 2019, respectively. The decrease in research and development expenses of $15.2 million was primarily due to expense reduction measures taken in response to COVID-19; in particular, a decrease of $13.2 million in development expenses for ZILRETTA due to a reduction in ZILRETTA life cycle management activities, a decrease of $1.5 million related to our portfolio expansion (including FX301) and other programs costs, and a decrease of $2.0 million in salary and other employee-related costs related to lower headcount. Those decreases were partially offset by an increase of $1.5 million in expenses related to FX201 clinical trial and related manufacturing activities.

Selling, General and Administrative Expenses

Selling, general and administrative expenses were $105.0 million and $129.7 million for the years ended December 31, 2020 and 2019, respectively. Selling expenses were $72.3 million and $96.3 million for the years ended December 31, 2020 and 2019. The year-over-year decrease in selling expenses of $24.0 million was primarily due to the expense reduction measures taken in response to COVID-19; in particular, the elimination of live presence at industry conferences, reductions in in-person physician speaker programs and reductions in select marketing programs and materials, as well as a reduction in travel expenses due to physician office limitations and travel guidelines and restrictions at the state and local level. General and administrative expenses were $32.7 million and $33.4 million for the years ended December 31, 2020 and 2019, respectively, which represents a decrease of $0.7 million.

Other Income (Expense)

Interest income was $0.9 million and $3.2 million for the years ended December 31, 2020 and 2019, respectively. The decrease in interest income was primarily due to a decrease in the average investment balance as well as a decrease in interest rates over the period.

Interest expense was $20.0 million and $17.1 million for the years ended December 31, 2020 and 2019, respectively. The increase in interest expense was due to the additional interest incurred associated with the term loan that we entered into in August 2019 under the amended credit and security agreement, as well as the revolving credit facility, which we drew down in February 2020.

We recorded other expense of $1.0 million for the year ended December 31, 2020, compared to other income of $0.4 million for the year ended December 31, 2019. The increase in other expense was primarily due to changes in the price of debt securities resulting in amortization of premiums rather than accretion of discounts as well as the loss from the disposal of equipment as noted in Note 8, partially offset by an increase in gains related to foreign currency exchange rates.

Income Taxes

The provision for income taxes for the year ended December 31, 2020, was comprised of $0.5 million in foreign withholding taxes related to the HK Tainuo upfront payment.

Liquidity and Capital Resources

During the year ended December 31, 2020, we generated $85.6 million in net product revenue. We have incurred significant net losses in each year since our inception in 2007, including net losses of $113.7 million, $149.8 million, and $169.7 million for fiscal years 2020, 2019, and 2018, respectively. As of December 31, 2020, we had an accumulated deficit of $782.3 million. We anticipate that we will continue to incur losses over the next few years.

Since our inception through December 31, 2020, we have funded our operations primarily through the sale of our common stock and convertible preferred stock and convertible debt, and through venture debt financing. From our inception through December 31, 2020, we had raised approximately $913 million from such transactions, including amounts from our initial and follow-on public offerings during 2014, 2016, 2017, and most recently in May of 2020, as well as our term loan facility

entered into in 2015 and 2019 and our 2024 Convertible Notes issuance in 2017. This funding is necessary to support the commercialization of ZILRETTA and to perform the research and development activities required to develop our other product candidates in order to generate future revenue streams. We may not be able to obtain financing on acceptable terms, or at all. In particular, as a result of the COVID-19 pandemic and actions taken to slow its spread, the global credit and financial markets have experienced extreme volatility and disruptions, including diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. If the equity and credit markets deteriorate, it may make any additional debt or equity financing more difficult, more costly and more dilutive.

In response to the economic and business disruption caused by COVID-19, in the second quarter of 2020, we undertook prudent and disciplined steps to reduce expenses across our organization, including hiring and travel freezes, suspension or termination of active clinical trials and deferral of select preclinical activities, reductions in in-person physician speaker programs, market research and select marketing programs, and elimination of non-essential operating expenses. As a result of these actions, our research and development and selling, general and administrative expenses were lower in 2020 as compared to the prior year. However, we expect that our research and development and selling, general and administrative expenses will increase in 2021 and beyond and, as a result, we may need additional capital to fund our operations, which we may seek to obtain through one or more equity offerings, debt and convertible debt financings, government or other third-party funding, and licensing or collaboration arrangements.

As of December 31, 2020, we had cash, cash equivalents and marketable securities of $175.3 million. Based on our current operating plan we anticipate that our existing cash, cash equivalents and marketable securities will fund our operations and debt obligations for at least the next twelve months from the date of issuance of the financial statements included in this report. Cash in excess of immediate requirements is invested in accordance with our investment policy, primarily with a view to capital preservation.

On August 2, 2019, we entered into an amended and restated credit and security agreement (the “amended and restated credit and security agreement”) with Silicon Valley Bank as agent, MidCap Financial Trust, Flexpoint MCLS Holdings, LLC, and the other lenders from time to time party thereto (collectively, the “Lenders”), providing for a term loan of $40.0 million and a revolving credit facility of up to $20.0 million, both of which mature on January 1, 2024. We concurrently borrowed the $40.0 million term loan and used $7.7 million of the proceeds to repay the remaining amount owed on our existing term loan with Silicon Valley Bank and MidCap Funding XIII Trust. In February 2020, we borrowed the full $20.0 million available under the revolving credit facility.

On May 18, 2020, we entered into an amendment to the amended and restated credit and security agreement (the “amendment”). Pursuant to the amendment, we borrowed $15.0 million under a new term loan advance and immediately used the proceeds to repay an equal amount under the revolving credit facility, and the maximum principal amount of the revolving credit facility was reduced from $20.0 million to $5.0 million. The new term loan is subject to substantially the same terms, including interest rate, amortization and maturity date, as the existing term loan under the credit facility. Additionally, if our liquidity (as defined in Note 10 of our accompanying consolidated financial statements) should decrease below $80.0 million, under the terms of the amended and restated credit and security agreement, we would become subject to a minimum revenue covenant. If we become subject to the minimum revenue covenant and fail to comply with it, the lenders could elect to declare all amounts outstanding to be immediately due and payable. Additionally, if our liquidity is below $80.0 million, all amounts received from customer collections will be applied immediately to reduce the revolving credit facility.

Term loan borrowings under the credit facility accrue interest monthly at a floating interest rate equal to the greater of the Prime Rate (as reported in the Wall Street Journal) plus 1.50% or 6.50% per annum. Under the term loan credit facility, following an 18-month interest-only period, principal will be due in 36 equal monthly installments commencing February 1, 2021, and ending on the Maturity Date. We may prepay the term loan at any time by paying the outstanding principal balance, a final payment equal to 6.75% of the term loan amount, all accrued interest and a prepayment fee of 3% of the outstanding term loan amount if repaid in the first year, 2% of the outstanding term loan amount if repaid in the second year, and 1% of the outstanding term loan amount if repaid in the third year of the loan; no prepayment fee is required thereafter.

Borrowings under the revolving credit facility accrue interest monthly at a floating interest rate equal to the greater of the Prime Rate (as reported in the Wall Street Journal) or 5.50% per annum. The revolving credit facility is co-terminus with the term loan. If the interest payment on the revolving credit facility is less than the amount of interest that would have been payable had we borrowed 25% of the total commitment under the revolving credit facility, or the Revolving Commitment Amount, then we will be required to pay the difference. We are also required to pay a facility fee in respect of the revolving credit facility equal to 1% of the Revolving Commitment Amount. We may retire the revolving credit facility early, at any time, by paying the outstanding principal balance, all accrued interest and a termination fee equal to 2% of the Revolving Commitment Amount if repaid in the first year, and 1% of the Revolving Commitment Amount if repaid in the second year; with no termination fee thereafter. To the extent any portion of the Revolving Commitment Amount is undrawn, we will be

required to pay an "unused line fee" equal to 0.25% per annum of the average unused portion of the Revolving Commitment Amount, calculated on a calendar year basis as an amount equal to the difference between (i) the Revolving Commitment Amount and (ii) the greater of (A) 25.0% of the Revolving Commitment Amount, and (B) the average for the period of the daily closing balance of the Revolving Commitment Amount outstanding.

On May 26, 2020, we completed an equity offering of our common stock, which resulted in the sale of 10,615,385 shares of our common stock at a price to the public of $9.75 per share including shares sold pursuant to the exercise in full of the underwriters' option to purchase additional shares. We received net proceeds from the equity offering of $96.8 million after deducting underwriting discounts, commissions, and offering costs.

On November 4, 2020, we entered into an Equity Distribution Agreement (the "Distribution Agreement") with Goldman Sachs & Co. LLC and Credit Suisse Securities (USA) LLC (collectively, the "Managers") relating to the issuance and sale from time to time of up to $100,000,000 of shares of our common stock. Under the terms of the Distribution Agreement, we will pay the Managers a commission of up to 3% of the gross sales price of any shares sold. No shares were sold under the Distribution Agreement as of December 31, 2020.

The following table shows a summary of our cash flows for each of the years ended December 31, 2020, 2019, and 2018:

	Year Ended December 31,		
(In thousands)	**2020**	**2019**	**2018**
Cash flows used in operating activities	$ (70,561)	$ (148,758)	$ (160,419)
Cash flows (used in) provided by investing activities	(22,763)	114,764	125,584
Cash flows provided by (used in) financing activities	118,775	29,018	(6,325)
Net increase (decrease) in cash, cash equivalents, and restricted cash	$ 25,451	$ (4,976)	$ (41,160)

Net Cash Used in Operating Activities

Operating activities used $70.6 million of cash in the year ended December 31, 2020. Cash used in operating activities resulted primarily from our net loss of $113.7 million, partially offset by changes in our operating assets and liabilities of $8.9 million and non-cash charges of $34.2 million. Changes in our operating assets and liabilities consisted primarily of a $7.1 million decrease in accounts receivable, a $0.3 million decrease in prepaid expenses and other current assets, and a $10.0 million increase in deferred revenue related to the license agreement with HK Tainuo, partially offset by a $0.8 million increase in inventory, a $6.3 million decrease in accounts payable and accrued expenses and a $1.3 million decrease in lease liabilities and other long-term liabilities primarily due to principal lease payments. Our non-cash charges consisted primarily of $18.6 million of stock-based compensation expense, $9.4 million related to the amortization of the debt discount and debt issuance costs related to the 2024 Convertible Notes, $2.5 million related to the provision for inventory, $1.6 million related to the amortization of right-of-use assets, $1.7 million of depreciation, $0.7 million related to non-cash interest expense related to amortization of the final payment due on the 2019 term loan, $0.2 of net amortization of premiums related to our investments, and $0.3 million related to the loss on disposal of fixed assets, partially offset by $0.7 million of premiums paid for the purchase of marketable securities.

Operating activities used $148.8 million of cash in the year ended December 31, 2019. Cash used in operating activities resulted primarily from our net loss of $149.8 million and changes in our operating assets and liabilities of $25.6 million, partially offset by non-cash charges of $26.6 million. Changes in our operating assets and liabilities consisted primarily of a $24.0 million increase in accounts receivable, a $7.7 million increase in inventory, partially offset by a $0.1 million decrease in prepaid expenses and other current assets, an increase of $7.0 million in accounts payable and accrued expenses and a $1.0 million decrease in lease liabilities and other long-term liabilities. Non-cash charges consisted primarily of $15.9 million of stock-based compensation expense, $8.7 million related to the amortization of the debt discount and debt issuance costs related to the 2024 Convertible Notes, $1.3 million related to the amortization of right-of-use assets, $1.1 million of depreciation and $0.9 million related to non-cash interest expense and loss from debt extinguishment related to our 2015 term loan, partially offset by $1.3 million of net accretion of discounts related to our investments.

Operating activities used $160.4 million of cash in the year ended December 31, 2018. Cash used in operating activities resulted primarily from our net loss of $169.7 million, offset by changes in our operating assets and liabilities of $14.2 million and non-cash charges of $23.4 million. Changes in our operating assets and liabilities consisted primarily of a $12.7 million increase in accounts receivable, a $5.2 million increase in inventory, and a $2.1 million increase in prepaid expenses and other current assets, partially offset by an increase of $5.8 million in accounts payable and accrued expenses. Non-cash charges consisted primarily of $15.5 million of stock-based compensation expense, $7.8 million related to the amortization of the debt discount and debt issuance costs related to the 2024 Convertible Notes, and $1.7 million of depreciation, partially offset by $1.3 million of net accretion of discounts related to our investments.

Net Cash (Used in) Provided by Investing Activities

Net cash used in investing activities was $22.8 million in the year ended December 31, 2020. Net cash used in investing activities consisted primarily of purchases of marketable securities of $79.6 million and capital expenditures of $10.1 million, primarily relating to the purchase of equipment associated with the expansion of our manufacturing facilities at Patheon. These expenses were partially offset by cash received for the redemption and sale of marketable securities of $66.9 million.

Net cash provided by investing activities was $114.7 million in the year ended December 31, 2019. Net cash provided by investing activities consisted primarily of cash received for the redemption and sale of marketable securities of $234.1 million, partially offset by cash used to purchase marketable securities of $115.5 million. In addition, $3.9 million of cash was used for capital expenditures, including $3.4 million for manufacturing equipment, $0.2 million for lab equipment and $0.3 million for leasehold improvements related to an expansion of our Burlington, Massachusetts headquarters.

Net cash provided by investing activities was $125.6 million in the year ended December 31, 2018. Net cash provided by investing activities consisted primarily of cash received for the redemption and sale of marketable securities of $348.9 million, partially offset by cash used to purchase marketable securities of $222.5 million. In addition, $0.8 million of cash was used for capital expenditures including $0.2 million for manufacturing equipment, $0.2 million for lab equipment and $0.4 million for leasehold improvements related to an expansion of our Burlington, Massachusetts headquarters.

Net Cash Provided by (Used in) Financing Activities

Net cash provided by financing activities was $118.8 million for the year ended December 31, 2020, of which $97.2 million related to the net proceeds received from the offering of our common stock, partially offset by public offering costs paid during the period of $0.4 million. We also received $1.9 million from the exercise of stock options and employee stock purchases through our employee stock purchase plan, as well as $20.0 million borrowed under the revolving credit facility associated with our 2019 term loan.

Net cash provided by financing activities was $29.0 million for the year ended December 31, 2019. Net cash provided by financing activities in the year ended December 31, 2019, consisted primarily of $40.0 million of gross proceeds received from the 2019 term loan facility and $3.5 million received from the exercise of stock options and employee stock purchases through our employee stock purchase plan, partially offset by $14.4 million related to the payment of principal on our 2015 term loan and $0.1 million of debt issuance costs related to the 2019 term loan facility.

Net cash used in financing activities was $6.3 million for the year ended December 31, 2018. Net cash used in financing activities in the year ended December 31, 2018, consisted primarily of $10.0 million related to the payment of our principal on our 2015 term loan, partially offset by $3.7 million received from the exercise of stock options and employee stock purchases through our employee stock purchase plan.

Contractual Obligations

The following table discloses aggregate information about our contractual obligations and the periods in which payments are due as of December 31, 2020:

	Payments Due By Period				
	Total	Less Than 1 Year	1 – 3 Years	3 – 5 Years	More Than 5 Years
	(in thousands)				
Long-term debt obligation (including interest)(1)	$ 70,461	$ 20,247	$ 39,941	$ 10,273	—
Operating lease obligations(2)	9,000	2,043	3,780	2,749	428
Monthly base fee to Patheon(3)	62,086	10,273	18,022	18,022	15,769
2024 Convertible notes obligations(4)	224,456	6,792	13,584	204,080	—
Supply Agreement with Evonik(5)	764	764	—	—	—
Total	$ 366,767	$ 40,119	$ 75,327	$ 235,124	$ 16,197

(1) Represents the contractually required principal and interest payments on our credit facility in accordance with the required payment schedule and the 6.75% final payment to the lender on January 1, 2024. Amounts associated with future interest payments to be made under the term loan were calculated using a floating interest rate equal to the greater of the prime rate plus 1.5% or 6.5% per annum and amounts associated with future interest payments to be made under the revolving credit facility were calculated using a floating interest rate equal to the greater of the prime rate or 5.50% per annum.

(2) Represents the contractually required payments under our operating lease obligations in existence as of December 31, 2020, in accordance with the required payment schedule. No assumptions were made with respect to renewing the lease terms at the expiration date of their initial terms. Refer to Note 14 – Commitments and Contingencies.

(3) Represents the contractually required monthly base fee to Patheon for the operation of the manufacturing suite.

(4) Represents the contractually required interest payments in accordance with the required payment schedule and the final principal payment of $201.3 million due on May 1, 2024.

(5) Represents contractually required purchases of PLGA for clinical and commercial supply of ZILRETTA. The required purchases are based upon a 24-month rolling forecast of 100% of our total volume requirements for the PLGA product. Only the first 12 months of the 24-month rolling forecast are binding. The required purchases are 50% of our total volume requirements for the PLGA product. Since the current required binding forecast does not go beyond December 2021, any potential minimum purchase in the year 2022 and beyond are not fixed or determinable and therefore no amounts are presented in the table above.

The table above reflects only payment obligations that are fixed or determinable. We enter into contracts in the normal course of business with CROs for clinical trials, with contract manufacturers for clinical and commercial supply manufacturing, and with vendors for preclinical research studies, research supplies and other services and products for operating purposes. These contracts generally provide for termination on notice, and therefore we believe that our non-cancelable obligations under these agreements are not material.

Off-Balance Sheet Arrangements

During the periods presented, we did not have, nor do we currently have, any off-balance sheet arrangements that are reasonably likely to have a current or future material effect on our financial condition, changes in financial condition, revenues or expenses, results of operations, liquidity, capital expenditures or capital resources.

Recent Accounting Pronouncements

A discussion of recent accounting pronouncements is included in Note 3 to the consolidated financial statements in this Annual Report on Form 10-K.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 10.0% change in interest rates would not have a material effect on the fair market value of our portfolio. Accordingly, we would not expect our operating results or cash flows to be affected to any significant degree by a sudden change in market interest rates on our investment portfolio.

- We have borrowed $55.0 million under our credit facility. Amounts outstanding under the credit facility bear interest at a floating interest rate equal to the greater of the prime rate plus 1.5% or 6.5% per annum.
- We have borrowed $201.3 million under the 2024 Convertible Notes. Amounts outstanding bear interest at a rate of 3.375% per annum. This is a fixed interest rate and thus we are not subject to interest rate risk in connection with the 2024 Convertible Notes.
- We do not believe that our cash, cash equivalents and marketable securities have significant risk of default or illiquidity. While we believe our cash and cash equivalents and certificates of deposit do not contain excessive risk, we cannot provide absolute assurance that in the future our investments will not be subject to adverse changes in market value. In addition, we maintain significant amounts of cash and cash equivalents at one or more financial institutions that are in excess of federally insured limits.

Most of our transactions are conducted in U.S. dollars. We do have certain material agreements with vendors located outside the United States, which have transactions conducted primarily in British Pounds and Euros. As of December 31, 2020, we had approximately $2.4 million in payables to vendors denominated in British pounds. A hypothetical 10% change in foreign exchange rates would result in a $0.2 million change in the value of our liabilities. No other payables to vendors were denominated in currencies other than in U.S. dollars. As of December 31, 2020, we also had an immaterial amount of cash denominated in British pounds. A hypothetical 10% change in foreign exchange rates would result in an immaterial change in the amount of cash denominated in British Pounds.

Item 8. Financial Statements and Supplementary Data

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of Flexion Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Flexion Therapeutics, Inc. and its subsidiary (the "Company") as of December 31, 2020 and 2019, and the related consolidated statements of operations and comprehensive loss, of changes in stockholders' (deficit) equity and of cash flows for each of the three years in the period ended December 31, 2020, including the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2020 and 2019, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2020 in conformity with accounting principles generally accepted in the United States of America.

Change in Accounting Principle

As discussed in Note 3 to the consolidated financial statements, the Company changed the manner in which it accounts for leases in 2019.

Basis for Opinion

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

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

Our audits included performing procedures to assess the risks of material misstatement of the 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. We believe that our audits provide a reasonable basis for our opinion.

Emphasis of Matter

As discussed in Note 1 to the consolidated financial statements, the Company is dependent on its ability to fund its operations through sales of ZILRETTA and/or raise additional capital, such as through debt or equity offerings, as needed. Also as discussed in Note 1 to the consolidated financial statements, the Company's debt facility includes a financial covenant. If the Company cannot grow sales of ZILRETTA in future periods, the Company may not maintain compliance with the revenue covenant and the Company could be required to repay its outstanding borrowings under the term loan and revolving credit facility. Management's plans in regard to these matters are described in Note 1.

Critical Audit Matters

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

Revenue recognition

As described in Note 3 to the consolidated financial statements, the Company primarily sells ZILRETTA to specialty distributors and a specialty pharmacy, who then subsequently resell ZILRETTA to physicians, clinics and certain medical centers or hospitals. Management recognizes revenue on product sales when the customer obtains control of the Company's product, which occurs at a point in time (upon delivery to the customer). Product revenues are recorded net of applicable reserves for variable consideration, including discounts and allowances. Components of variable consideration include trade discounts and allowances, product returns, government chargebacks, discounts and rebates, and other incentives. These reserves are based on the amounts earned, or to be claimed on the related sales, and are classified as reductions of accounts receivable (if the amount is payable to the customer) or a current liability (if the amount is payable to a party other than a customer). Product revenue, net for the year ended December 31, 2020 was $85.6 million, while total product revenue allowances and reserves was $4.7 million as of December 31, 2020.

The principal considerations for our determination that performing procedures relating to revenue recognition is a critical audit matter are the significant audit effort in performing procedures and in evaluating audit evidence obtained related to net revenue recognized on product sales.

Addressing the matter involved performing procedures and evaluating audit evidence in connection with forming our overall opinion on the consolidated financial statements. These procedures included, among others (i) testing, on a sample basis, whether the criteria for revenue recognition have been met by obtaining and inspecting the customer order information, the related customer contract, and proof of delivery; (ii) testing the completeness and accuracy of the amount of variable consideration, including service fees and allowances and purchaser/provider discounts and rebates; (iii) evaluating the completeness and accuracy of the inputs in management's variable consideration calculations, including the customer sales amounts and the terms of the respective underlying contract or rebate offering; and (iv) agreeing, on a sample basis, variable consideration amounts earned to subsequent payments to the customers.

/s/ PricewaterhouseCoopers LLP
Boston, Massachusetts
March 10, 2021

We have served as the Company's auditor since 2010.

Flexion Therapeutics, Inc.

Consolidated Balance Sheets

(In thousands, except share amounts)

	December 31, 2020	December 31, 2019
Assets		
Current assets		
Cash and cash equivalents	$ 107,704	$ 82,253
Marketable securities	67,576	54,407
Accounts receivable, net	30,025	37,115
Inventories	15,394	16,529
Prepaid expenses and other current assets	5,112	5,371
Total current assets	225,811	195,675
Property and equipment, net	19,538	13,662
Right-of-use assets	6,577	8,223
Total assets	$ 251,926	$ 217,560
Liabilities and Stockholders' Deficit		
Current liabilities		
Accounts payable	$ 6,928	$ 15,258
Accrued expenses and other current liabilities	20,008	19,610
Deferred revenue	10,000	—
Operating lease liabilities	1,526	1,351
Current portion of long-term debt	16,806	—
Total current liabilities	55,268	36,219
Long-term operating lease liability, net	6,123	7,609
Long-term debt, net	44,114	40,176
2024 convertible notes, net	162,786	153,413
Other long-term liabilities	295	251
Total liabilities	268,586	237,668
Commitments and contingencies		
Preferred Stock, $0.001 par value; 10,000,000 shares authorized at December 31, 2020 and December 31, 2019 and 0 shares issued and outstanding at December 31, 2020 and December 31, 2019	—	—
Stockholders' deficit		
Common stock, $0.001 par value; 100,000,000 shares authorized; 49,403,034 and 38,361,476 shares issued and outstanding, at December 31, 2020 and December 31, 2019, respectively	49	38
Additional paid-in capital	765,607	648,391
Accumulated other comprehensive (loss) income	(11)	62
Accumulated deficit	(782,305)	(668,599)
Total stockholders' deficit	(16,660)	(20,108)
Total liabilities and stockholders' deficit	$ 251,926	$ 217,560

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

Flexion Therapeutics, Inc.

Consolidated Statements of Operations and Comprehensive Loss

(In thousands, except per share amounts)

	Year Ended December 31,		
	2020	**2019**	**2018**
Revenues			
Product revenue, net	$ 85,552	$ 72,957	$ 22,524
Operating expenses			
Cost of sales	19,249	9,960	7,336
Research and development	54,326	69,559	53,079
Selling, general and administrative	104,996	129,709	121,311
Total operating expenses	178,571	209,228	181,726
Loss from operations	(93,019)	(136,271)	(159,202)
Other (expense) income			
Interest income	876	3,212	4,567
Interest expense	(20,027)	(17,066)	(15,712)
Other (expense) income	(1,041)	352	688
Total other (expense) income	(20,192)	(13,502)	(10,457)
Loss before income taxes	(113,211)	(149,773)	(169,659)
Income tax expense	495	—	—
Net loss	$ (113,706)	$ (149,773)	$ (169,659)
Net loss per common share, basic and diluted	$ (2.53)	$ (3.93)	$ (4.49)
Weighted average common shares outstanding, basic and diluted	45,013	38,086	37,751
Other comprehensive (loss) income			
Unrealized (losses) gains from available-for-sale securities, net of tax of $0	(73)	139	330
Total other comprehensive (loss) income	(73)	139	330
Comprehensive loss	$ (113,779)	$ (149,634)	$ (169,329)

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

Flexion Therapeutics, Inc.

Consolidated Statements of Changes in Stockholders' (Deficit) Equity

(In thousands)

	Common Stock					
	Shares	Par Value	Additional Paid-in Capital	Accumulated Other Comprehensive (Loss) Income	Accumulated Deficit	Total Stockholders' (Deficit) Equity
Balance at December 31, 2017	37,611	$ 38	$ 609,810	$ (407)	$ (349,167)	$ 260,274
Issuance of common stock for equity awards, net of shares withheld for taxes	197		1,653			1,653
Employee stock purchase plan	138		2,022			2,022
Stock-based compensation expense			15,459			15,459
Net loss			—		(169,659)	(169,659)
Other comprehensive income			—	330		330
Balance at December 31, 2018	37,946	$ 38	$ 628,944	$ (77)	$ (518,826)	$ 110,079
Issuance of common stock for equity awards, net of shares withheld for taxes	230		1,726			1,726
Employee stock purchase plan	185		1,820			1,820
Stock-based compensation expense			15,901			15,901
Net loss					(149,773)	(149,773)
Other comprehensive income				139		139
Balance at December 31, 2019	38,361	$ 38	$ 648,391	$ 62	$ (668,599)	$ (20,108)
Issuance of common stock net of issuance costs	10,615	$ 10	$ 96,754			96,764
Issuance of common stock for equity awards, net of shares withheld for taxes	272	$ 1	284			285
Employee stock purchase plan	155		1,601			1,601
Stock-based compensation expense			18,577			18,577
Net loss					(113,706)	(113,706)
Other comprehensive loss				(73)		(73)
Balance at December 31, 2020	49,403	$ 49	$ 765,607	$ (11)	$ (782,305)	$ (16,660)

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

Flexion Therapeutics, Inc.
Consolidated Statements of Cash Flows
(In thousands)

	Year Ended December 31,		
	2020	**2019**	**2018**
Cash flows from operating activities			
Net loss	$ (113,706)	$ (149,773)	$ (169,659)
Adjustments to reconcile net loss to cash used in operating activities:			
Depreciation	1,696	1,059	1,714
Amortization of right-of-use assets	1,646	1,337	—
Stock-based compensation expense	18,577	15,901	15,459
Provision for inventory	2,540	—	—
Non-cash interest expense	744	564	—
Amortization (accretion) of premium (discount) on marketable securities	205	(1,337)	(1,320)
Loss on disposal of fixed assets	262	—	—
Loss from debt extinguishment	—	352	—
Amortization of debt discount and debt issuance costs	9,373	8,714	7,805
Premium paid on securities purchased	(728)	(34)	(214)
Changes in operating assets and liabilities:			
Accounts receivable	7,090	(23,994)	(12,711)
Inventory	(922)	(7,674)	(5,244)
Prepaid expenses and other current assets	259	126	(2,097)
Accounts payable	(6,560)	1,702	5,141
Accrued expenses and other current liabilities	274	5,326	707
Deferred revenue	10,000	—	—
Lease liabilities	(1,311)	(1,027)	—
Net cash used in operating activities	(70,561)	(148,758)	(160,419)
Cash flows from investing activities			
Purchases of property and equipment	(10,069)	(3,894)	(852)
Proceeds from sale of fixed assets	25	—	—
Purchases of marketable securities	(79,617)	(115,466)	(222,482)
Sale and redemption of marketable securities	66,898	234,124	348,918
Net cash (used in) provided by investing activities	(22,763)	114,764	125,584
Cash flows from financing activities			
Proceeds from borrowings under term loan	15,000	40,000	—
Payment of debt issuance costs	—	(161)	—
Proceeds from revolving line of credit	20,000	—	—
Repayments of revolving line of credit	(15,000)	—	—
Proceeds from the offering of common stock	97,289	—	—
Payments of public offering costs	(400)	—	—
Payments on notes payable	—	(14,367)	(10,000)
Proceeds from the exercise of stock options	285	1,726	1,653
Proceeds from employee stock purchase plan	1,601	1,820	2,022
Net cash provided by (used in) financing activities	118,775	29,018	(6,325)
Net increase (decrease) in cash, cash equivalents, and restricted cash	25,451	(4,976)	(41,160)
Cash, cash equivalents, and restricted cash at beginning of period	82,253	87,229	128,389
Cash, cash equivalents, and restricted cash at end of period	$ 107,704	$ 82,253	$ 87,229
Supplemental disclosures of cash flow information			
Cash paid for interest	$ 10,412	$ 8,049	$ 7,874
Non-cash investing and financing activities			
Right-of-use asset obtained in exchange for operating lease obligation	$ —	$ 9,560	$ —
Purchases of property and equipment in accounts payable and accrued expenses	$ 432	$ 2,202	$ 986
Public offering costs in accounts payable and accrued expenses	$ 125	$ —	$ —

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

1. Nature of the Business

Flexion Therapeutics, Inc. ("Flexion" or the "Company") was incorporated under the laws of the state of Delaware on November 5, 2007. Flexion is a biopharmaceutical company focused on the discovery, development and commercialization of novel, local therapies for the treatment of patients with musculoskeletal conditions, beginning with osteoarthritis, ("OA"), a type of degenerative arthritis. The Company has an approved product, ZILRETTA®, which it markets in the United States. ZILRETTA is the first and only extended-release, intra-articular, or IA (meaning in the joint), injection indicated for the management of OA knee pain. ZILRETTA is a non-opioid therapy that employs Flexion's proprietary microsphere technology to provide effective pain relief. The pivotal Phase 3 trial, on which the approval of ZILRETTA was based, showed that ZILRETTA met the primary endpoint of pain reduction at Week 12, with statistically significant pain relief extending through Week 16. The Company also has two pipeline programs focused on the local treatment of musculoskeletal conditions: FX201, which is an investigational IA gene therapy product candidate in clinical development for the treatment of OA, and FX301, a preclinical product candidate, which is being developed as a locally administered peripheral nerve block for control of post-operative pain.

The Company is subject to risks and uncertainties common to companies in the biopharmaceutical industry, including, but not limited to, new technological innovations, dependence on key personnel, protection of proprietary technology, compliance with government regulations, and the ability to secure additional capital to fund operations. Successfully commercializing ZILRETTA requires significant sales and marketing efforts and the Company's pipeline programs may require significant additional research and development efforts, including extensive preclinical and clinical testing. These activities will in turn require significant amounts of capital, qualified personnel and adequate infrastructure. There can be no assurance when, if ever, the Company will realize significant revenue from the sales of ZILRETTA or if the development efforts supporting the Company's pipeline, including future clinical trials, will be successful.

The accompanying consolidated financial statements have been prepared on a basis which assumes that the Company will continue as a going concern and which contemplates the realization of assets and satisfaction of liabilities and commitments in the normal course of business. The Company has incurred recurring losses and negative cash flows from operations. As of December 31, 2020, the Company had cash, cash equivalents, and marketable securities of approximately $175.3 million.

The Company's operations have been and continue to be affected by the ongoing global pandemic of a novel strain of coronavirus ("COVID-19") and the resulting volatility and uncertainty it has caused. In March 2020, the World Health Organization declared COVID-19 a pandemic and recommended containment and mitigation measures worldwide. The COVID-19 pandemic has caused significant volatility and uncertainty, which could result in a prolonged economic downturn that has disrupted and is expected to continue disrupt the Company's business. While there have been no material asset impairments recorded to date, any prolonged material future disruptions to the work of the Company's employees, suppliers, contract manufacturers, or vendors, or to the operations of physicians that administer ZILRETTA could negatively impact the Company's operations, availability of supplies, carrying value of assets, operating results or cash flows.

In the Company's Quarterly Report on Form 10-Q for the three months ended March 31, 2020, the Company disclosed that there was substantial doubt about its ability to continue as a going concern as a result of conditions that existed as of March 31, 2020. Specifically, those conditions included an expected material decline in revenue due to COVID-19 as compared to its prior expectations, and as a result, it was deemed probable that the Company would fail to meet the revenue covenant within the Company's amended and restated credit and security agreement described in Note 10. In the months following March, 31, 2020, the Company took certain actions designed to alleviate the substantial doubt, including reducing certain operating expenses through hiring and travel freezes, suspension and/or termination of active clinical trials, reduction of certain marketing expenses, and elimination of non-essential operating expenses, modifying the amended and restated credit and security agreement, and completing an equity offering of 10,615,385 shares of the Company's common stock which resulted in $96.8 million of net proceeds to the Company. Additionally, while purchases of ZILRETTA by physicians, clinics, and certain medical centers or hospitals (*i.e.*, healthcare providers who administer ZILRETTA to patients) initially dropped precipitously in the latter part of March into early April due to the adverse impact of COVID-19 on the operations of these healthcare providers, as the second quarter progressed, there was an increase in demand for ZILRETTA such that total ZILRETTA purchases by healthcare providers for the second quarter were consistent with the first quarter of 2020. The Company experienced continued growth in purchases of ZILRETTA by healthcare providers in the second half of 2020 and ended the year with total net revenue of $85.6 million. Based on the actions the Company took as described above, in the second quarter of 2020, the Company disclosed that it had alleviated the substantial doubt about its ability to continue as a going concern. Management believes that current cash, cash equivalents, and marketable securities on hand at December 31, 2020, will be sufficient to fund operations and debt obligations for at least the next 12 months from the issuance date of these

financial statements. As of December 31, 2020, the Company was in compliance with all covenants under the amended and restated credit and security agreement.

The future viability of the Company is dependent on its ability to fund its operations through sales of ZILRETTA and/or raise additional capital, such as through debt or equity offerings, as needed. If the Company is unable to grow sales of ZILRETTA in future periods, it is possible that the Company may not maintain compliance with the revenue covenant, in the event it applies, in future periods. As a result, the Company could be required to repay its outstanding borrowings under the term loan and revolving credit facility and would seek additional financing. The Company may not be able to obtain financing on acceptable terms, or at all. In particular, as a result of the COVID-19 pandemic and actions taken to slow its spread, the global credit and financial markets have experienced extreme volatility and disruptions, including diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. If the equity and credit markets deteriorate, it may make any additional debt or equity financing more difficult, more costly and more dilutive. If the Company is unable to obtain funding on a timely basis, the Company may need to curtail its operations, including the commercialization of ZILRETTA, and/or reduce the scope of, or delay certain research and development activities including the FX201 or FX301 pipeline programs, which could adversely affect its prospects.

2. Financing Transactions

On November 4, 2020, the Company entered into the Distribution Agreement with Goldman Sachs & Co. LLC and Credit Suisse Securities (USA) LLC (collectively, the "Managers") relating to the issuance and sale from time to time by the Company, through the Managers, of up to $100,000,000 of shares of the Company's common stock. Under the terms of the Distribution Agreement, the Company will pay the Managers a commission of up to 3% of the gross sales price of any shares sold. As of December 31, 2020, no shares had been issued or sold under the Distribution Agreement.

On May 26, 2020, the Company completed an equity offering of its common stock, which resulted in the sale of 10,615,385 shares of its common stock at a price to the public of $9.75 per share including shares sold pursuant to the exercise in full of the underwriters' option to purchase additional shares. The Company received net proceeds from the equity offering of $96.8 million after deducting underwriting discounts, commissions, and offering costs.

On August 2, 2019, the Company entered into an amended and restated credit and security agreement (the "amended and restated credit and security agreement") with Silicon Valley Bank as agent, MidCap Financial Trust, Flexpoint MCLS Holdings, LLC, and the other lenders from time to time party thereto (collectively, the "Lenders"), providing for a term loan of $40.0 million and a revolving credit facility of up to $20.0 million, both of which mature on January 1, 2024 (the "Maturity Date"). The Company concurrently borrowed the $40.0 million term loan and used $7.7 million of the proceeds to repay the remaining amount owed on the 2015 term loan. In February 2020, the Company drew down the full $20.0 million available under the revolving credit facility. On May 18, 2020, the Company entered into an amendment to the amended and restated credit and security agreement (the "amendment"). Pursuant to the amendment, the Company borrowed $15.0 million under a new term loan advance and immediately used the proceeds to repay an equal amount under the revolving credit facility, and the maximum principal amount of the revolving credit facility was reduced from $20.0 million to $5.0 million. The new term loan is subject to substantially the same terms, including interest rate, amortization and maturity date, as the existing term loan under the credit facility.

3. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying consolidated financial statements have been prepared in accordance with the rules and regulations of the Securities and Exchange Commission (the "SEC") and Generally Accepted Accounting Principles ("GAAP") for financial information, including the accounts of the Company and its wholly owned subsidiary after elimination of all significant intercompany accounts and transactions.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and judgments that may affect the reported amounts of assets and liabilities, revenues and expenses and related disclosures. The Company bases estimates and judgments on historical experience and on various other factors that it believes to be reasonable under the circumstances. The most significant estimates in these consolidated financial statements include estimates related to revenue recognition and accrued expenses related to preclinical and clinical development costs. The Company's actual results may differ from these estimates under different assumptions or conditions. The Company evaluates its estimates on an ongoing basis. Changes in estimates are reflected in reported results in the period in which they become known by the Company's management.

The full extent to which the COVID-19 pandemic will directly or indirectly impact the Company's business, results of operations and financial condition, including sales, expenses, reserves and allowances, clinical trials, research and development costs and employee-related amounts, will depend on future development that are highly uncertain, including as a result of new information that may emerge concerning COVID-19 and the actions taken to contain or treat it, as well as the economic impact on local, regional, national and international customers and markets. The Company has made estimate of the impact of COVID-19 within its financial statements and there may be changes to those estimates in future periods.

Revenue Recognition

The Company recognizes revenue in accordance with Accounting Standards Codification ("ASC") Topic 606 - *Revenue from Contracts with Customers* ("Topic 606"). Under Topic 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to be entitled to in exchange for those goods or services.

To determine revenue recognition for arrangements that an entity determines are within the scope of Topic 606, the entity performs the following five steps: (i) identify the contract(s) with a customer, (ii) identify the performance obligations in the contract, (iii) determine the transaction price, (iv) allocate the transaction price to the performance obligations in the contract, and (v) recognize revenue when (or as) the entity satisfies a performance obligation. The Company only applies the five-step model to arrangements that meet the definition of a contract with a customer under Topic 606, including when it is probable that the entity will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of Topic 606, the Company assesses the goods or services promised within each contract, determines those that are performance obligations, and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

Product Revenue, Net— The Company primarily sells ZILRETTA to specialty distributors and a specialty pharmacy, who then subsequently resell ZILRETTA to physicians, clinics and certain medical centers or hospitals. The Company also contracts directly with healthcare providers and intermediaries such as Group Purchasing Organizations ("GPOs"). In addition, the Company enters into arrangements with government payers that provide for government mandated rebates and chargebacks with respect to the purchase of ZILRETTA.

The Company recognizes revenue on product sales when the customer obtains control of the Company's product, which occurs at a point in time (upon delivery to the customer). The Company has determined that the delivery of ZILRETTA to its customers constitutes a single performance obligation. There are no other promises to deliver goods or services beyond what is specified in each accepted customer order. The Company has assessed the existence of a significant financing component in the agreements with its customers. The trade payment terms with our customers do not exceed one year and therefore the Company has elected to apply the practical expedient and no amount of consideration has been allocated as a financing component. Product revenues are recorded net of applicable reserves for variable consideration, including discounts and allowances.

Transaction Price, including Variable Consideration— Revenues from product sales are recorded at the net sales price (transaction price), which includes estimates of variable consideration for which reserves are established. Components of variable consideration include trade discounts and allowances, product returns, government chargebacks, discounts and rebates, and other incentives, such as voluntary patient assistance, and other fee for service amounts that are detailed within contracts between the Company and its customers relating to the Company's sale of its products. These reserves, as detailed below, are based on the amounts earned, or to be claimed on the related sales, and are classified as reductions of accounts receivable (if the amount is payable to the customer) or a current liability (if the amount is payable to a party other than a customer). These estimates take into consideration a range of possible outcomes which are probability-weighted in accordance with the expected value method in Topic 606 for relevant factors such as current contractual and statutory requirements, specific known market events and trends, industry data, and forecasted customer buying and payment patterns. Overall, these reserves reflect the Company's best estimates of the amount of consideration to which it is entitled based on the terms of the respective underlying contracts.

The amount of variable consideration which is included in the transaction price may be constrained and is included in the net sales price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized under the contract will not occur in a future period. Actual amounts of consideration ultimately received may differ from the Company's estimates. If actual results in the future vary from the Company's original estimates, the Company will adjust these estimates, which would affect net product revenue and earnings in the period such variances become known.

Service Fees and Allowances—The Company compensates its customers and GPOs for sales order management, data, and distribution services. However, the Company has determined such services received to date are not distinct from the Company's sale of products to the customer and, therefore, these payments have been recorded as a reduction of revenue

within the statement of operations and comprehensive loss through December 31, 2020, as well as a reduction to trade receivables, net on the consolidated balance sheets.

Product Returns— Consistent with industry practice, the Company generally offers customers a limited right of return for product that has been purchased from the Company based on the product's expiration date. The Company estimates the amount of its product sales that may be returned by its customers and records this estimate as a reduction of revenue in the period the related product revenue is recognized, as well as within accrued expenses and other current liabilities, net, on the consolidated balance sheets. The Company currently estimates product return liabilities using available industry data and its own sales information, including its visibility into the inventory remaining in the distribution channel. The Company has received an immaterial amount of returns to date and believes that returns of ZILRETTA will be minimal.

Chargebacks— Chargebacks for fees and discounts to qualified government healthcare providers represent the estimated obligations resulting from contractual commitments to sell products to qualified VA hospitals and 340b entities at prices lower than the list prices charged to customers who directly purchase the product from the Company. The 340b Drug Discount Program is a US federal government program created in 1992 that requires drug manufacturers to provide outpatient drugs to eligible health care organizations and covered entities at significantly reduced prices. Customers charge the Company for the difference between what they pay for the product and the statutory selling price to the qualified government entity. These reserves are established in the same period that the related revenue is recognized, resulting in a reduction of product revenue and trade receivables, net. Chargeback amounts are generally determined at the time of resale to the qualified government healthcare provider by customers, and the Company generally issues credits for such amounts within a few weeks of the Customer's notification to the Company of the resale. Reserves for chargebacks consist of credits that the Company expects to issue for units that remain in the distribution channel inventories at each reporting period-end that the Company expects will be sold to qualified healthcare providers, and chargebacks that customers have claimed, but for which the Company has not yet issued a credit.

Government Rebates— The Company is subject to discount obligations under state Medicaid programs and Medicare. These reserves are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability which is included in accrued expenses and other current liabilities on the consolidated balance sheets. For Medicare, the Company also estimates the number of patients in the prescription drug coverage gap for whom the Company will owe an additional liability under the Medicare Part D program. The Company anticipates its exposure to utilization from the Medicare Part D coverage gap discount program to be immaterial. For Medicaid programs, the Company estimates the portion of sales attributed to Medicaid patients and records a liability for the rebates to be paid to the respective state Medicaid programs. The Company's liability for these rebates consists of invoices received for claims from prior quarters that have not been paid or for which an invoice has not yet been received, estimates of claims for the current quarter, and estimated future claims that will be made for product that has been recognized as revenue, but which remains in the distribution channel inventories at the end of each reporting period.

Purchaser/Provider Discounts and Rebates—Beginning in the third quarter of 2019, the Company began offering rebates to eligible purchasers and healthcare providers that are variable based on the volume of product purchased. Rebates are based on actual purchase levels during the rebate purchase period. The Company estimates these rebates and records such estimate in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability.

Other Incentives— Other incentives which the Company offers include voluntary patient assistance programs, such as the co-pay assistance program, which are intended to provide financial assistance to qualified commercially-insured patients with prescription drug co-payments required by payers. The calculation of the accrual for co-pay assistance is based on an estimate of claims and the cost per claim that the Company expects to receive associated with product that has been recognized as revenue but remains in the distribution channel inventories at the end of each reporting period. The adjustments are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability which is included as a component of accrued expenses and other current liabilities on the consolidated balance sheets.

The following table summarizes activity in each of the product revenue allowance and reserve categories for the years ended December 31, 2020, 2019, and 2018:

(In thousands)	Service Fees, Allowances and Chargebacks	Government Rebates and Other Incentives	Product Returns	Purchaser/Provider Discounts and Rebates	Total
Balance as of December 31, 2017	$ 60	$ 15	$ 2	—	$ 77
Provision related to sales in the current year	1,688	502	124	—	2,314
Credit or payments made during the period	(1,147)	(26)	(1)	—	(1,174)
Balance as of December 31, 2018	601	491	125	—	1,217
Provision related to sales in the current year	5,527	261	334	2,685	8,807
Credit or payments made during the period	(4,281)	(375)	(57)	(1,029)	(5,742)
Adjustments related to prior period sales	—	(129)	—	—	(129)
Balance as of December 31, 2019	1,847	248	402	1,656	4,153
Provision related to sales in the current year	7,660	1,090	499	4,633	13,882
Credit or payments made during the period	(7,774)	(903)	(139)	(4,457)	(13,273)
Adjustments related to prior period sales	—	95	(134)	—	(39)
Balance as of December 31, 2020	$ 1,733	$ 530	$ 628	$ 1,832	$ 4,723

License Agreement – On March 30, 2020, the Company entered into an exclusive license agreement with Hong Kong Tainuo Pharma Ltd. (“HK Tainuo”) and Jiangsu Tainuo Pharmaceutical Co. Ltd. (“Jiangsu Tainuo”), a subsidiary of China Shijiazhuang Pharmaceutical Co, Ltd. for the development and commercialization (other than manufacturing) of ZILRETTA in Greater China (consisting of mainland China, Hong Kong and Macau, and Taiwan). Under the terms of the agreement, HK Tainuo paid the Company an upfront payment of $10.0 million, of which $5.0 million was received as of June 30, 2020, and the remaining $5.0 million was received as of September 30, 2020. The Company is also eligible to receive up to $32.5 million in aggregate development, regulatory and commercial sales milestone payments. All payments received from HK Tainuo are subject to the applicable Hong Kong withholding taxes. HK Tainuo is responsible for the clinical development, product registration and commercialization of ZILRETTA in Greater China and Jiangsu Tainuo serves as the guarantor of HK Tainuo’s obligations and responsibilities under the agreement. The Company is solely responsible for the manufacture and supply of ZILRETTA to HK Tainuo for all clinical and commercial activities. The terms related to product manufacturing and supply, including pricing and minimum purchase requirements agreed to in the license agreement, will be covered by a separate supply agreement, which has not yet been finalized. All amounts owed to the Company are nonrefundable and non-creditable once paid. Unless terminated earlier in accordance with its terms, the license agreement continues in effect in perpetuity or as long as HK Tainuo or Jiangsu Tainuo continue to sell ZILRETTA in Greater China. Either party may terminate the agreement prior to expiration in the event of a material breach if not cured within 60 days from the date of notice of such breach (30 days in the case of payment obligations), or either party files for bankruptcy. The Company also has the right to terminate the agreement if HK Tainuo, Jiangsu Tainuo or any affiliate of each commences any action or proceeding that challenges the validity, enforceability or scope of any Company patent in Greater China. Upon any such termination, the license granted to HK Tainuo will terminate and all know-how and patents will revert back to the Company. The Company concluded that the license and supply obligations were not distinct performance obligations, and therefore the transaction price will be recognized as revenue as the Company’s supply obligation is fulfilled over the term of the supply agreement, which has not yet commenced. No revenue was recognized associated with this contract as of December 31, 2020.

Inventory

The Company values its inventories at the lower of cost or estimated net realizable value. The Company determines the cost of its inventories, which includes amounts related to materials and manufacturing overhead, on a first-in, first-out basis. The Company performs an assessment of the recoverability of capitalized inventory during each reporting period, and it writes down any excess and obsolete inventories to their estimated realizable value in the period in which the impairment is first identified. Such impairment charges, should they occur, are recorded within cost of sales. The determination of whether inventory costs will be realizable requires estimates by management. If actual market conditions are less favorable than projected by management, additional write-downs of inventory may be required, which would be recorded as a cost of sales in the consolidated statements of operations and comprehensive loss.

The Company capitalizes inventory costs associated with the Company’s products after regulatory approval when, based on management’s judgment, future commercialization is considered probable and the future economic benefit is expected to be realized. Inventory acquired prior to receipt of marketing approval of a product candidate is expensed as research and development expense as incurred. Inventory that can be used in either the production of clinical or commercial product is expensed as research and development expense when selected for use in a clinical manufacturing campaign. Inventory produced that will be used in promotional marketing campaigns is expensed to selling, general and administrative expense when it is selected for use in a marketing program.

Consolidation

The accompanying consolidated financial statements include the Company and its wholly-owned subsidiary, Flexion Therapeutics Securities Corporation. The Company has eliminated all intercompany transactions for the years ended December 31, 2020, 2019, and 2018. In addition, Flexion Therapeutics, Inc. is registered to do business in the United Kingdom through its branch office located in Swindon, United Kingdom.

Accounts Receivable

Accounts receivable are recorded net of customer allowances for distribution fees and chargebacks, and doubtful accounts. Allowances for distribution fees and chargebacks are based on contractual terms. The Company estimates the allowance for doubtful accounts based on existing contractual payment terms, actual payment patterns of its customers and individual customer circumstances. At December 31, 2020, the Company determined that an allowance for doubtful accounts was not required. No accounts were written off during the year ended December 31, 2020.

Cash and Cash Equivalents

The Company considers all highly liquid investments with a maturity of three months or less at the date of purchase to be cash equivalents. The Company currently invests available cash in money market funds of a major financial institution, corporate bonds, government obligations and commercial paper.

Marketable Securities

Marketable securities consist of investments with original maturities greater than ninety days and less than one year from the balance sheet date. Long-term investments consist of investments with maturities of greater than one year. The Company classifies all of its investments, which consist solely of debt securities, as available-for-sale. Accordingly, these investments are recorded at fair value, which is based on quoted market prices. Unrealized gains and losses are recorded as a component of other comprehensive income (loss). Realized gains and losses are determined on a specific identification basis and are included in other income (loss). Amortization and accretion of discounts and premiums is recorded in other income.

Property and Equipment

Property and equipment are stated at cost less accumulated depreciation. Depreciation and amortization expense is recognized using the straight-line method over the following estimated useful lives:

	Estimated Useful Life (Years)
Computers, office equipment, and minor computer software	3
Computer software	7
Manufacturing equipment	7-10
Furniture and fixtures	5

Leasehold improvements are amortized over the shorter of the lease term or the estimated useful life of the related asset. Costs of major additions and betterments are capitalized and depreciated on a straight-line basis over their useful lives. Repairs and maintenance costs are expensed as incurred. Upon retirement or sale, the cost of assets disposed of and the related accumulated depreciation are removed from the accounts and any resulting gain or loss is credited or charged to income. Property and equipment includes construction-in-progress, that is not yet in service.

Foreign Currencies

The Company maintains a bank account designated in British Pounds. All foreign currency payables and cash balances are measured at the applicable exchange rate at the end of the reporting period. All associated gains and losses from foreign currency transactions are reflected in the consolidated statements of operations.

Leases

In February 2016, the Financial Accounting Standards Board, or FASB, issued ASU 2016-02, *Leases* (“ASU 2016-02”), to increase transparency and comparability among organizations by recognizing lease assets and liabilities, including operating leases, on the balance sheet and disclosing key information about leasing arrangements.

The Company adopted ASU 2016-02 on January 1, 2019, using the “Comparatives under 840” approach, which was approved by the FASB in July 2018 as part of ASU 2018-11. Under this method, the consolidated financial statements as of the year ended December 31, 2020 and 2019, are presented applying the new requirements under ASC 842, while the consolidated financial statements as of the year ended December 31, 2018, are presented under ASC 840.

As part of its adoption of ASU 2016-02, the Company elected the package of practical expedients which allowed it to not reassess (1) whether existing contracts contained leases, (2) the lease classification for existing leases, and (3) whether existing initial direct costs met the new definition. Consequently, on adoption, the Company recognized lease liabilities of $7.0 million and corresponding right-of-use ("ROU") assets of $6.6 million based on the present value of the remaining minimum rental payments under current leasing standards for existing operating leases. These lease liabilities and ROU assets relate to operating leases only, as the Company concluded that it does not have any finance leases. The difference between the lease liability and the ROU assets upon adoption relates to the deferred rent balance that had been recorded prior to adoption. The Company determined that no cumulative adjustment to retained earnings was required.

The Company determines if an arrangement is a lease at contract inception. Operating lease assets represent a right to use an underlying asset for the lease term and operating lease liabilities represent an obligation to make lease payments arising from the lease. Operating lease liabilities with a term greater than one year and their corresponding right-of-use assets are recognized on the balance sheet at the commencement date of the lease based on the present value of lease payments over the expected lease term. Certain adjustments to the right-of-use asset may be required for items such as initial direct costs paid or incentives received. The Company made an accounting policy election to expense leases with a term of one year or less on a straight-line basis over the lease term. To date, the Company has not identified any material short-term leases, either individually or in the aggregate.

As the Company's leases do not provide an implicit rate, the Company utilized the appropriate incremental borrowing rate, which is the rate incurred to borrow on a collateralized basis over a similar term an amount equal to the lease payments in a similar economic environment. The Company estimated the incremental borrowing rate based on a yield curve analysis of companies with a similar credit rating to its own, which was calculated using a number of financial ratios and qualitative considerations of the Company's business. The yields on the Company's currently outstanding debt (the convertible senior notes and term loan described below) were also used as inputs to the analysis to calculate a spread, adjusted for factors that reflect the profile of secured borrowing over the expected term of the lease.

The components of a lease should be split into three categories: lease components (*e.g.*, land, building, etc.), non-lease components (*e.g.*, common area maintenance, utilities, performance of manufacturing services, purchase of inventory, etc.), and non-components (*e.g.*, property taxes, insurance, etc.). Then the fixed contract consideration (including any related to non-components) must be allocated based on fair values to the lease components and non-lease components. Although separation of lease and non-lease components is required, certain practical expedients are available to entities. Entities electing the practical expedient would not separate lease and non-lease components. Rather, they would account for each lease component and the related non-lease component together as a single component. The Company has elected to use this practical expedient for its real estate leases and account for each lease component and related non-lease component as one single component. In contrast, the Company has elected not to apply the practical expedient for its lease of manufacturing space at Patheon and has instead allocated consideration between the lease and non-lease components of the contract. The Company calculated the fair value of the lease component using publicly available information to identify comparable rentals in the same geographic area. The remainder of the consideration was allocated to the non-lease components.

Impairment of Long-Lived Assets

The Company reviews its long-lived assets, including property and equipment, for impairment whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Factors that the Company considers in deciding when to perform an impairment review include significant underperformance of the business in relation to expectations, significant negative industry or economic trends, and significant changes or planned changes in the use of the assets. If an impairment review is performed to evaluate a long-lived asset for recoverability, the Company compares forecasts of undiscounted cash flows expected to result from the use and eventual disposition of the long-lived asset to its carrying value. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of an asset are less than its carrying amount. The impairment loss would be based on the excess of the carrying value of the impaired asset over its fair value, determined based on discounted cash flows.

Debt Issuance Costs, net

As of December 31, 2020 and 2019, the carrying value of debt issuance costs was $2.3 million and $2.9 million, respectively, and was presented as a direct deduction from the carrying amounts of long-term debt. In addition, $0.6 million, $0.6 million, and $0.4 million, respectively, of debt issuance costs were amortized and recognized as other expense in the statement of operations for the years ended December 31, 2020, 2019, and 2018.

Research and Development Expenses

Research and development expenses are comprised of costs incurred in performing research and development activities, including salaries and benefits, facilities costs, overhead costs, depreciation, clinical trial and related clinical manufacturing

costs, contract services and other related costs. Research and development costs are expensed to operations as the related obligation is incurred.

As part of the process of preparing its financial statements, the Company is required to estimate its accrued expenses. This process involves reviewing open contracts and purchase orders, communicating with applicable internal and vendor personnel to identify services that have been performed on the Company's behalf and estimating the level of service performed and the associated cost incurred for the service when the Company has not yet been invoiced or otherwise notified of the actual cost. The majority of the Company's service providers invoice it monthly in arrears for services performed or when contractual milestones are met. The Company makes estimates of its accrued expenses as of each balance sheet date in its financial statements based on facts and circumstances known to it at that time. The Company periodically confirms the accuracy of its estimates with the service providers and makes adjustments if necessary. Examples of estimated accrued research and development expenses include fees paid to:

- CROs in connection with clinical studies;
- investigative sites in connection with clinical studies;
- vendors related to product manufacturing, development and distribution of clinical supplies; and
- vendors in connection with preclinical development activities.

The Company records expenses related to clinical studies and manufacturing development activities based on its estimates of the services received and efforts expended pursuant to contracts with multiple CROs and manufacturing vendors that conduct and manage these activities on the Company's behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract, and may result in uneven payment flows.

The Company makes estimates of its accrued expenses as of each balance sheet date in its financial statements based on facts and circumstances known to it. If timelines or contracts are modified based upon changes in the clinical trial protocol or scope of work to be performed, the Company modifies its estimates of accrued expenses accordingly on a prospective basis. If the Company does not identify costs that it has begun to incur, or if it underestimates or overestimates the level of services performed or the costs of these services, the Company's actual expenses could differ from its estimates. To date, the Company has not adjusted its estimates at any particular balance sheet date in any material amount.

Patent Costs

All patent-related costs incurred in connection with filing and prosecuting patent applications are recorded as general and administrative expenses as incurred, as recoverability of such expenditures is uncertain.

Accounting for Stock-Based Compensation

The Company measures all stock options and other stock based-awards granted to employees and non-employees at the fair value at the date of grant using the Black-Scholes option-pricing model. The fair value of the awards is recognized as expense over the requisite service period, which is generally the vesting period of the respective award. The straight-line method of expense recognition is applied to all awards with service-only conditions. The Company accounts for forfeitures as they occur and does not estimate future forfeitures. As such, previously recognized compensation expense for an award is reversed in the period that the award is forfeited. For stock awards that have a performance condition, the Company recognizes compensation expense based on its assessment of the probability that the performance condition will be achieved, using an accelerated attribution model, over the explicit or implicit service period.

The Company classifies stock-based compensation expense in the consolidated statements of operations in the same manner in which the award recipient's payroll costs are classified, or in the case of a non-employee, in the same manner as the award recipient's service costs are classified.

Concentration of Credit Risk and Significant Suppliers

Financial instruments that potentially expose the Company to concentration of credit risk consist primarily of commercial paper and corporate bonds. The Company generally invests its cash in money market funds, government and corporate bonds, and commercial paper at one financial institution. The Company does not believe that it is subject to unusual credit risk beyond the normal credit risk associated with commercial banking relationships.

The Company is completely dependent on third-party manufacturers and product suppliers for research and commercial activities. In particular, the Company relies on a limited number of manufacturers and relies on them to purchase from third-party suppliers the materials necessary to produce its product candidates for its clinical trials and for commercial supply. These programs would be adversely affected by a significant interruption in the supply of active pharmaceutical ingredients.

Gross product revenues and accounts receivable from each of the Company's customers who individually accounted for 10% or more of total gross products revenues and/or 10% or more of total accounts receivable consisted of the following:

	Percent of Total Gross Product Revenues			Percent of Accounts Receivable	
	Year Ended December 31,			As of December 31,	
	2020	2019	2018	2020	2019
Customer A	36%	44%	57%	37%	41%
Customer B	20%	24%	31%	21%	20%
Customer C	26%	15%	—	21%	20%
Customer D	<10%	<10%	<10%	<10%	11%

No other customers accounted for more than 10% of product revenue or accounts receivable for the years ended December 31, 2020, 2019, and 2018, respectively.

Comprehensive Loss

Comprehensive loss includes net loss as well as other changes in stockholders' equity that result from transactions and economic events other than those with stockholders. The Company's only element of other comprehensive income (loss) in all periods presented was unrealized gains (losses) on available-for-sale securities.

Income Taxes

The Company accounts for income taxes using the asset and liability method. Under this method, deferred tax assets and liabilities are recognized for the estimated future tax consequences of events that have been recognized in the financial statements or in the Company's tax returns. Deferred taxes are determined based on the differences between financial statement carrying amounts of existing assets and liabilities and their respective tax basis. Deferred tax assets and liabilities are measured using enacted rates in effect for the year in which these temporary differences are expected to be recovered or settled. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes. The Company assesses the likelihood that its deferred tax assets will be recovered from future taxable income and, to the extent it believes, 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 a charge to income tax expense. Potential recovery of deferred tax assets is evaluated by estimating the future taxable profits expected and considering prudent and feasible tax planning strategies.

The Company accounts for uncertainty in income taxes recognized in the financial statements by applying a two-step process to determine the amount of tax benefit to be recognized. First, the tax position must be evaluated to determine the likelihood that it will be sustained upon external examination by the taxing authorities. If the tax position is deemed more-likely-than-not to be sustained, the tax position is then assessed to determine the amount of benefit to recognize in the financial statements. The amount of benefit that may be recognized is the largest amount that has a greater than 50% likelihood of being realized upon ultimate settlement. The provision for income taxes includes the effects of any resulting tax reserves, or unrecognized tax benefits, that are considered appropriate as well as the related net interest and penalties.

Fair Value Measurements

Fair value is defined as the exchange price that would be received to sell an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants at the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

- Level 1 — Quoted market prices in active markets for identical assets or liabilities. Level 1 consists primarily of financial instruments whose value is based on quoted market prices, such as exchange-traded instruments and listed equities.
- Level 2 — Observable inputs (other than Level 1 quoted prices) such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.
- Level 3 — Unobservable inputs that are supported by little or no market activity and that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

The Company's financial instruments consist of cash equivalents, marketable securities, its term loan and 2024 Convertible Notes (Note 10). The estimated fair value of the Company's financial instruments, with the exception of the 2024 Convertible Notes, approximates their carrying values.

The fair value of the 2024 Convertible Notes, which differs from their carrying value, is influenced by interest rates, stock price and stock price volatility and is determined by prices for the 2024 Convertible Notes observed in market trading. The market for trading of the 2024 Convertible Notes is not considered to be an active market and therefore the estimate of fair value is based on Level 2 inputs. The estimated fair value of the 2024 Convertible Notes, face value of $201.3 million, was $182.3 million at December 31, 2020.

Net Loss Per Share

The Company follows the two-class method when computing net loss per share as the Company has issued shares that meet the definition of participating securities. The two-class method determines net loss per share for each class of common and participating securities according to dividends declared or accumulated and participation rights in undistributed earnings. The two-class method requires income available to common stockholders for the period to be allocated between common and participating securities based on their respective rights to receive dividends as if all income for the period had been distributed.

Basic net loss per share attributable to common stockholders is computed by dividing the net loss attributable to common stockholders by the weighted average number of shares of common stock outstanding for the period. Diluted net loss attributable to common stockholders is computed by adjusting net loss attributable to common stockholders to reallocate undistributed earnings based on the potential impact of dilutive securities, including the assumed conversion of our 2024 Convertible Notes, outstanding stock options and unvested restricted common stock, except where the result would be anti-dilutive. Diluted net loss per share attributable to common stockholders is computed by dividing the diluted net loss attributable to common stockholders by the weighted average number of common shares outstanding for the period, including potential dilutive common shares assuming the dilutive effect of the conversion of the 2024 Convertible Notes, the exercise of outstanding stock options and the vesting unvested restricted common stock. In the diluted net loss per share calculation, net loss would also be adjusted for the elimination of interest expense on the 2024 Convertible Notes, if the impact was not anti-dilutive. For periods in which the Company has reported net losses, diluted net loss per share attributable to common stockholders is the same as basic net loss per share attributable to common stockholders, since dilutive common shares are not assumed to have been issued if their effect is anti-dilutive. Potential common shares will always be anti-dilutive for periods in which the Company has reported a net loss. Diluted net loss per share attributable to common stockholders is the same as basic net loss per share attributable to common stockholders for the years ended December 31, 2020, 2019, and 2018.

Segment Data

The Company manages its operations as a single operating segment for the purposes of assessing performance and making operating decisions. The Company is a biopharmaceutical company focused on the development and commercialization of novel, local therapies. All revenues for the years ended December 31, 2020 and 2019, were generated in the United States.

Recent Accounting Pronouncements

Accounting Standards Recently Adopted

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments - Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments* (“ASU 2016-13”). The new standard requires entities to measure all expected credit losses for financial assets held at the reporting date based on historical experience, current conditions and reasonable and supportable forecasts. ASU 2016-13 is effective for fiscal years, and the interim periods within those years, beginning after December 15, 2019, and early adoption is permitted. The Company adopted this standard as of January 1, 2020. The adoption of ASU 2016-13 did not have a material impact on the Company’s condensed consolidated financial statements.

In July 2018, the FASB issued ASU No. 2018-13, *Fair Value Measurement (Topic 820): Disclosure Framework—Changes to the Disclosure Requirements for Fair Value Measurement* (“ASU 2018-13”). The new standard modifies the disclosure requirements on fair value measurements in Topic 820, Fair Value Measurement, as part of the FASB’s disclosure framework project. ASU 2018-13 is effective for fiscal years, and the interim periods within those years, beginning after December 15, 2019, and early adoption is permitted. Additionally, the new standard permits an entity to early adopt any removed or modified disclosures upon issuance of the ASU and delay adoption of the additional disclosures until their effective date. ASU 2018-13 removes the requirement to disclose the amount of and reasons for transfers between Level 1 and Level 2 of the fair value hierarchy. The Company early adopted this portion of the standard as the quarter ended September 30, 2018. The Company adopted the remainder of the standard as of January 1, 2020. The adoption of the remainder of ASU 2018-13 did not have a material impact on the Company’s condensed consolidated financial statements.

Accounting Standards Recently Issued

In August 2020, the FASB issued ASU No. 2020-06, *Debt – Debt with Conversion and Other Options* ("ASU 2020-06"). The new standard simplifies the accounting for certain financial instruments with characteristics of liabilities and equity. The new guidance reduced the number of accounting models for convertible debt and convertible preferred stock instruments and made certain disclosure amendments intended to improve the information provided to users. The guidance also amended the derivative guidance for the "own stock" scope exception, which exempts qualifying instruments from being accounted for as derivatives if certain criteria are met. Finally, the standard changed the way certain convertible instruments are treated when calculating earnings per share. The standard is effective for the Company for fiscal years, and the interim periods within those years, beginning after December 15, 2021, and early adoption is permitted. The Company is currently evaluating the impact of ASU 2020-06 on the Company's consolidated financial statements.

4. Fair Value of Financial Assets and Liabilities

The following tables present information about the Company's assets that are measured at fair value on a recurring basis as of December 31, 2020 and 2019, and indicate the level of the fair value hierarchy utilized to determine such fair value:

	Fair Value Measurements as of December 31, 2020			
(In thousands)	**Level 1**	**Level 2**	**Level 3**	**Total**
Assets:				
Cash equivalents	$ 79,148	$ 6,832	$ —	$ 85,980
Marketable securities	—	67,576	—	67,576
	$ 79,148	$ 74,408	$ —	$ 153,556

	Fair Value Measurements as of December 31, 2019			
(In thousands)	**Level 1**	**Level 2**	**Level 3**	**Total**
Assets:				
Cash equivalents	$ —	$ 69,733	$ —	$ 69,733
Marketable securities	—	54,407	—	54,407
	$ —	$ 124,140	$ —	$ 124,140

As of December 31, 2020, the Company's cash equivalents and marketable securities that are invested in money market funds are valued using Level 1 inputs based on quoted prices for identical securities in active markets. The Company measures the fair value of certain marketable securities using Level 2 inputs and primarily relies on quoted prices in active markets for similar marketable securities. Amortization and accretion of discounts and premiums are recorded in other income. As of December 31, 2019, the Company's cash equivalents, and marketable securities were classified within Level 2 of the fair value hierarchy due to the inputs utilized.

The Company had a term loan outstanding under its 2015 credit facility with MidCap Financial Funding XIII Trust and Silicon Valley Bank (the "2015 term loan"). On August 2, 2019, the Company entered into an amended and restated credit and security agreement with Silicon Valley Bank as agent, MidCap Financial Trust, and Flexpoint MCLS Holdings, LLC (collectively, the "Lenders"), providing for a term loan of $40.0 million (the "2019 term loan"). The Company concurrently borrowed the $40.0 million term loan and used $7.7 million of the proceeds to repay the remaining amount owed on the 2015 term loan. In February 2020, the Company drew down the full $20.0 million available under the revolving credit facility. On May 18, 2020, the Company entered into an amendment to the amended and restated credit and security agreement (the "amendment"). Pursuant to the amendment, the Company borrowed $15.0 million under a new term loan advance and immediately used the proceeds to repay an equal amount under the revolving credit facility, and the maximum principal amount of the revolving credit facility was reduced from $20.0 million to $5.0 million. The new term loan is subject to substantially the same terms, including interest rate, amortization and maturity date, as the existing term loan under the credit facility. The amount outstanding on the 2019 term loan is reported at its carrying value in the accompanying balance sheet as of December 31, 2020. The Company determined the fair value of the 2019 term loan using an income approach that utilizes a discounted cash flow analysis based on current market interest rates for debt issuances with similar remaining years to maturity, adjusted for credit risk. The 2019 term loan was valued using Level 2 inputs as of December 31, 2020. The results of the calculation yielded a fair value that approximates its carrying value. The Company also concluded that the carrying value of the revolving credit facility approximated fair value because of the short-term maturity of this debt instrument.

On May 2, 2017, the Company issued 3.375% convertible senior notes due 2024 (the "2024 Convertible Notes") with embedded conversion features. The Company estimated the fair value of the 2024 Convertible Notes using a discounted cash flow approach to derive the value of a debt instrument using the expected cash flows and the estimated yield related to the convertible notes. The significant assumptions used in estimating the expected cash flows were: the estimated market yield based on an implied yield and credit quality analysis of a term loan with similar attributes, and the average implied volatility of the Company's traded and quoted options available as of May 2, 2017. The Company recorded approximately

$136.7 million as the fair value of the liability on May 2, 2017, with a corresponding amount recorded as a discount on the initial issuance of the 2024 Convertible Notes of approximately $64.5 million. The debt discount was recorded to equity and is being amortized to the debt liability over the life of the 2024 Convertible Notes using the effective interest method.

The fair value of the 2024 Convertible Notes, which differs from their carrying value, is influenced by interest rates, stock price and stock price volatility and is determined by prices for the 2024 Convertible Notes observed in market trading. The market for trading of the 2024 Convertible Notes is not considered to be an active market and therefore the estimate of fair value is based on Level 2 inputs. The estimated fair value of the 2024 Convertible Notes, face value of $201.3 million, was $182.3 million at December 31, 2020.

5. Marketable Securities

As of December 31, 2020 and 2019, the fair value of available-for-sale marketable securities by type of security was as follows:

	December 31, 2020			
(In thousands)	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Commercial paper	$ 6,890	$ —	$ —	$ 6,890
U.S. government obligations	9,997	1	—	9,998
Corporate bonds	50,700	2	(14)	50,688
	$ 67,587	$ 3	$ (14)	$ 67,576

	December 31, 2019			
(In thousands)	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Commercial paper	$ 6,189	$ —	$ —	$ 6,189
U.S. government obligations	29,950	24	—	29,974
Corporate bonds	18,206	38	—	18,244
	$ 54,345	$ 62	$ —	$ 54,407

As of December 31, 2020 and 2019, marketable securities consisted of approximately $67.6 million and $54.4 million, respectively, of investments that mature within 12 months. There were no investments with maturities greater than 12 months as of December 31, 2020, and December 31, 2019. The Company assesses its available-for-sale marketable securities for impairment on a quarterly basis in accordance with ASU No. 2016-13, *Financial Instruments - Credit Losses* (Topic 326): Measurement of Credit Losses on Financial Instruments. There were no material impairments of the Company's available-for-sale marketable securities measured and carried at fair value during the year ended December 31, 2020.

6. Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consisted of the following as of December 31, 2020 and 2019:

	December 31,	
(in thousands)	2020	2019
Prepaid expenses	$ 4,346	$ 5,072
Deposits	112	61
Interest receivable on marketable securities	246	238
Other	408	—
Total prepaid expenses and other current assets	$ 5,112	$ 5,371

7. Inventory

Inventory consisted of the following as of December 31, 2020 and 2019:

	December 31,	
(In thousands)	2020	2019
Raw materials	$ 4,287	$ 2,846
Work in process	4,666	7,575
Finished goods	6,441	6,108
Total inventories	$ 15,394	$ 16,529

Finished goods manufactured by the Company have a shelf life of approximately 24 months from the date of manufacture.

The Company reduces its inventory to net realizable value for potentially excess, dated or obsolete inventory based on an analysis of forecasted demand compared to quantities on hand and any firm purchase orders, as well as product shelf life. During the year ended December 31, 2020, the Company expensed $8.1 million to cost of sales for unabsorbed manufacturing and overhead costs related to the operation of the United Kingdom facility at Patheon UK Limited. In addition, cost of sales for the year ended December 31, 2020, included a charge of $2.5 million resulting from a write-down of short-dated ZILRETTA inventory. The charge was estimated based on an analysis of the remaining shelf life of the Company's inventory at the time that inventory is forecasted to be sold. The inventory charge represents excess inventory which the Company does not expect to be able to sell due to the short dating.

8. Property and Equipment, Net

Property and equipment, net, as of December 31, 2020 and 2019, consisted of the following:

	December 31,	
(In thousands)	**2020**	**2019**
Computer and office equipment	$ 1,203	$ 1,184
Manufacturing equipment	12,297	12,147
Furniture and fixtures	609	609
Software	495	455
Leasehold improvements	1,157	1,157
Construction—in progress	13,924	6,077
	29,685	21,629
Less: Accumulated depreciation	(10,147)	(7,967)
Total property and equipment, net	$ 19,538	$ 13,662

Depreciation expense for the years ended December 31, 2020, 2019, and 2018, was $1.7 million, $1.1 million, and $1.7 million, respectively. For the year ended December 31, 2020, the Company disposed of one piece of equipment and recorded a loss on the disposal of $0.3 million. There was no property or equipment disposed of during the year ended December 31, 2019. As of December 31, 2020, construction in progress consists primarily of equipment purchases related to the expansion of the Company's manufacturing capabilities at its contract manufacturer, Patheon U.K. Limited.

9. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities consisted of the following as of December 31, 2020 and 2019:

	December 31,	
(In thousands)	**2020**	**2019**
Research and development	$ 1,856	$ 1,924
Payroll and other employee-related expenses	10,674	8,748
Professional services fees	2,094	4,888
Accrued interest	1,464	1,356
Product revenue reserves	2,990	2,306
Accrual for employee stock purchase plan	235	183
Other	695	205
Total accrued expenses and other current liabilities	$ 20,008	$ 19,610

10. Debt

Amended and Restated Credit and Security Agreement

Term Loan

On August 4, 2015, the Company entered into a credit and security agreement with MidCap Financial Trust, as agent, and MidCap Financial Funding XIII Trust and Silicon Valley Bank, as lenders, to borrow up to $30.0 million in term loans. On August 2, 2019, the Company terminated the credit and security agreement and concurrently entered into an amended and restated credit and security agreement (the "amended and restated credit and security agreement") with Silicon Valley Bank as agent, MidCap Financial Trust, Flexpoint MCLS Holdings, LLC, and the other lenders from time to time party thereto (collectively, the "Lenders"), providing for a term loan of $40.0 million and a revolving credit facility of up to $20.0 million, both of which mature on January 1, 2024 (the "Maturity Date"). The Company concurrently borrowed the $40.0 million term loan and used $7.7 million of the proceeds to repay the remaining amount owed on the 2015 term loan.

The Company granted the Lenders a security interest in substantially all of its personal property, rights and assets, other than intellectual property, to secure the payment of all amounts owed under the amended and restated credit and security agreement. The Company agreed not to encumber any of its intellectual property without the Lender's prior written consent.

The amended and restated credit and security agreement contains certain representations, warranties, and covenants of the Company, including a minimum revenue covenant that will be in effect at any time the Company's liquidity (defined as cash and cash equivalents and marketable securities held with Silicon Valley Bank and certain accounts receivables as deemed eligible under the amended and restated credit and security agreement) is below $80.0 million. Additionally, if the Company's liquidity is below $80.0 million, all amounts received from customers collections will be applied immediately to reduce the revolving credit facility. As filed in the Form 8-K issued by the Company on May 18, 2020, prior to May 2021, the minimum revenue covenant, if it applies in the future, is set annually and is based on the greater of (i) a conservative percent of that year's approved forecast and (ii) modest growth over the trailing twelve months of actual revenues. Beginning in May 2021, the minimum revenue covenant, if it applies, will be the greatest of (i) a conservative percentage of that year's approved forecast, (ii) modest growth over the trailing twelve months of actual revenues and (iii) 100% of the minimum revenue covenant amount for the preceding month.

On May 18, 2020, the Company borrowed $15.0 million under a new term loan advance and immediately used the proceeds to repay an equal amount under the revolving credit facility, and the maximum principal amount of the revolving credit facility was reduced from $20.0 million to $5.0 million. The new term loan is subject to substantially the same terms, including interest rate, amortization and maturity dates, as the existing term loan under the credit facility.

The amended and restated credit and security agreement also has a material adverse event clause. If the revenue covenant becomes applicable and the Company fails to comply with it, or a material adverse change as defined in the agreement occurs, the amounts due under the amended and restated credit and security agreement could be declared immediately due and payable. As of December 31, 2020, the Company was compliant with all covenants.

Term loan borrowings under the credit facility accrue interest monthly at a floating interest rate equal to the greater of the prime rate plus 1.5% or 6.5% per annum. Following an interest-only period of 18 months, principal is due in 36 equal monthly installments commencing February 1, 2021, and ending on the Maturity Date. Upon the Maturity Date, the Company will be obligated to pay a final payment equal to 6.75% of the total principal amounts borrowed under the facility. The final payment amount is being accreted to the carrying value of the debt using the straight-line method, which approximates the effective interest method. As of December 31, 2020, the carrying value of the term loan was approximately $55.9 million, of which, $16.8 million is due within 12 months and $39.1 million is due in greater than 12 months.

The Company may prepay the term loan at any time by paying the outstanding principle balance, a final payment equal to 6.75% of the term loan amount, all accrued interest and a prepayment fee of 3% of the outstanding term loan amount if repaid in the first year, 2% of the outstanding term loan amount if repaid in the second year, and 1% of the outstanding term loan amount if repaid in the third year of the loan; no prepayment fee is required thereafter.

As of December 31, 2020, annual principal and interest payments due under the term loan are as follows:

Year		**Aggregate Minimum Payments** *(in thousands)*
2021		19,968
2022		20,296
2023		19,088
2024		5,249
Thereafter		—
Total	$	64,601
Less interest		(5,889)
Less unamortized portion of final payment		(2,792)
Total	$	55,920

Revolving Credit Facility

Borrowings under the revolving credit facility accrue interest monthly at a floating interest rate equal to the greater of the prime rate or 5.50% per annum. In addition to paying interest on any amounts borrowed under the revolving credit facility, the Company owes an unused revolving line facility fee equal to 0.25% per annum of the average unused portion of the revolving line, multiplied by the difference between the total amount available to be borrowed (the "Revolving Commitment Amount") and the greater of the average outstanding revolver balance and 25% of the Commitment Amount. The revolving credit facility and any related fees or interest payments was made available to the Company beginning January 1, 2020, and in February 2020, the Company drew down the $20.0 million available. On May 18, 2020, the Company repaid $15.0 million

of the outstanding principal balance, and the maximum principal amount of the revolving credit facility was reduced from $20.0 million to $5.0 million.

Beginning on January 1, 2020, if the interest payment on the revolving credit facility is less than the amount of interest that would have been payable had the Company borrowed 25% of the Revolving Commitment Amount, then the Company will be required to pay the difference.

The Company may retire the revolving credit facility early, at any time, by paying the outstanding principal balance, all accrued interest and a termination fee equal to 2% of the Revolving Commitment Amount if repaid in the first year, and 1% of the Revolving Commitment Amount if repaid in the second year; with no termination fee thereafter.

2024 Convertible Notes

On May 2, 2017, the Company issued an aggregate of $201.3 million principal amount of the 2024 Convertible Notes. The 2024 Convertible Notes have a maturity date of May 1, 2024, are unsecured and accrue interest at a rate of 3.375% per annum, payable semi-annually on May 1 and November 1 of each year, beginning November 1, 2017. The Company received $194.8 million in proceeds for the sale of the 2024 Convertible Notes, after deducting fees and expenses of $6.5 million.

Upon conversion of the 2024 Convertible Notes, at the election of each holder of a 2024 Convertible Note (the "Holder"), the note will be convertible into cash, shares of the Company's common stock, or a combination thereof, at the Company's election (subject to certain limitations in the 2015 term loan), at a conversion rate of approximately 37.3413 shares of common stock per $1,000 principal amount of the 2024 Convertible Notes, which corresponds to an initial conversion price of approximately $26.78 per share of the Company's common stock.

The conversion rate is subject to adjustment from time to time upon the occurrence of certain events, including, but not limited to, fundamental change events and certain corporate events that occur prior to the maturity date of the notes. In addition, if the Company delivers a notice of redemption, the Company will increase, in certain circumstances, the conversion rate for a Holder who elects to convert its notes in connection with such a corporate event or notice of redemption, as the case may be. At any time prior to the close of business on the business day immediately preceding February 1, 2024, Holders may convert all, or any portion, of the 2024 Convertible Notes at their option only under the following circumstances:

(1) during any calendar quarter commencing after the calendar quarter ending on June 30, 2017 (and only during such calendar quarter), if the last reported sale price of the Company's common stock for at least 20 trading days (whether or not consecutive) during a period of 30 consecutive trading days ending on the last trading day of the immediately preceding calendar quarter is greater than or equal to 130% of the conversion price on each applicable trading day;

(2) during the five business day period after any ten consecutive trading day period (the "measurement period") in which the trading price per $1,000 principal amount of notes for each trading day of the measurement period was less than 98% of the product of the last reported sale price of the Company's common stock and the conversion rate on each such trading day;

(3) if the Company calls any or all of the notes for redemption, at any time prior to the close of business on the business day immediately preceding the redemption date; and

(4) upon the occurrence of specified corporate events.

On or after February 1, 2024, until the close of business on the business day immediately preceding the maturity date, Holders may convert their notes at any time, regardless of the foregoing circumstances. The Company may redeem, for cash, all or any portion of the 2024 Convertible Notes, at its option, on or after May 6, 2020, if the last reported sale price of the Company's common stock has been at least 130% of the conversion price for at least 20 trading days during any 30 consecutive day trading period, at a redemption price equal to 100% of the principal amount of the 2024 Convertible Notes to be redeemed, plus accrued and unpaid interest, subject to the Holders' right to convert as described above.

The 2024 Convertible Notes are considered convertible debt with a cash conversion feature. Per ASC 470-20, *Debt with Conversion and Other Options*, the Company has separated the convertible debt into liability and equity components based on the fair value of a similar debt instrument excluding the embedded conversion option. The carrying amount of the liability component was calculated by measuring the fair value of a similar liability that does not have an associated convertible feature. The allocation was performed in a manner that reflected our non-convertible debt borrowing rate for similar debt. The equity component of the 2024 Convertible Notes was recognized as a debt discount and represents the difference between the proceeds from the issuance of the 2024 Convertible Notes and the fair value of the liability of the 2024 Convertible Notes on their respective dates of issuance. The excess of the principal amount of the liability component over its carrying amount ("debt discount") is amortized to interest expense using the effective interest method over seven years. The

equity component is not re-measured as long as it continues to meet the conditions for equity classification. The liability component of $136.7 million was recorded as long-term debt at May 2, 2017, with the remaining equity component of $64.5 million recorded as additional paid-in capital.

In connection with the issuance of the 2024 Convertible Notes, the Company incurred approximately $6.5 million of debt issuance costs, which primarily consisted of underwriting, legal and other professional fees, and allocated these costs to the liability and equity components based on the allocation of the proceeds. Of the total debt issuance costs, $4.4 million were allocated to the liability component and are recorded as a reduction of the 2024 Convertible Notes in our consolidated balance sheets. The remaining $2.1 million was allocated to the equity component and is recorded as a reduction to additional paid-in capital.

Debt discount and issuance costs of $68.9 million are being amortized to interest expense over the life of the 2024 Convertible Notes using the effective interest rate method. As of December 31, 2020, the stated interest rate was 3.375%, and the effective interest rate was 9.71%. Interest expense related to the 2024 Convertible Notes for the year ended December 31, 2020, was $15.6 million, including $8.8 million related to amortization of the debt discount.

The table below summarizes the carrying value of the 2024 Convertible Notes as of December 31, 2020:

		(in thousands)
Gross proceeds	$	201,250
Portion of proceeds allocated to equity component (additional paid-in capital)		(64,541)
Debt issuance costs		(6,470)
Portion of issuance costs allocated to equity component (additional paid-in capital)		2,075
Amortization of debt discount and debt issuance costs		30,472
Carrying value 2024 Convertible Notes	$	162,786

11. Stockholders' Equity

On February 17, 2014, the Company filed an amended and restated Certificate of Incorporation (the "Restated Certificate") in connection with the closing of the Company's initial public offering. As of December 31, 2020, under the Restated Certificate, the Company is authorized to issue 10,000,000 shares of preferred stock with a par value of $0.001 per share.

On June 7, 2016, the Company completed a follow-on public offering of its common stock, which resulted in the sale of 5,900,000 shares of the Company's common stock at a price to the public of $14.00 per share including shares sold pursuant to the exercise in full of the underwriters' option to purchase additional shares.

On November 15, 2016, the Company completed a follow-on public offering of its common stock, which resulted in the sale of 4,140,000 shares of the Company's common stock at a price to the public of $18.00 per share including shares sold pursuant to the exercise in full of the underwriters' option to purchase additional shares.

On October 16, 2017, the Company completed a follow-on public offering of its common stock, which resulted in the sale of 5,520,000 shares of the Company's common stock at a price to the public of $25.50 per share including shares sold pursuant to the exercise in full of the underwriters' option to purchase additional shares.

On May 26, 2020, the Company completed an equity offering of the Company's common stock, which resulted in the sale of 10,615,385 shares of the Company's common stock at a price to the public of $9.75 per share including shares sold pursuant to the exercise in full of the underwriters' option to purchase additional shares.

On November 4, 2020, the Company entered into the Distribution Agreement with the Managers relating to the issuance and sale from time to time by the Company, through the Managers, of up to $100,000,000 of shares of the Company's common stock. Under the terms of the Distribution Agreement, the Company will pay the Managers a commission of up to 3% of the gross sales price of any shares sold. As of December 31, 2020, no shares had been issued or sold under the Distribution Agreement.

Each share of common stock entitles the holder to one vote on all matters submitted to a vote of the Company's stockholders. Common stockholders are entitled to receive dividends, as may be declared by the board of directors, if any, subject to the preferential dividend rights of any holders of Preferred Stock. As of December 31, 2020, no dividends have been declared.

12. Stock Plans

2013 Equity Incentive Plan

On January 27, 2014, the Company's stockholders approved the 2013 Equity Incentive Plan (the "2013 Plan"), which became effective on February 11, 2014, the date of execution of the underwriting agreement pursuant to which the Company's common stock was priced for its initial public offering. Prior to the effective date of the 2013 Plan, the Company granted stock-based awards pursuant to the 2009 Stock Incentive Plan (the "2009 Plan), which had similar features to the 2013 Plan. The 2013 Plan provides for the grant of incentive stock options ("ISOs"), non-statutory stock options, stock appreciation rights, restricted stock awards, restricted stock unit awards, performance-based stock awards, and other forms of equity compensation. Initially, the maximum number of shares of the Company's common stock that may be issued pursuant to stock awards under the 2013 Plan was 2,337,616, which is the sum of (i) 1,230,012 shares, plus (ii) the number of shares remaining available for grant under the 2009 Plan, plus (iii) any shares subject to outstanding stock options or other stock awards that would have otherwise returned to the 2009 Plan (such as upon the expiration or termination of a stock award prior to vesting). Additionally, the number of shares of common stock reserved for issuance under the 2013 Plan automatically increases on January 1 of each year, beginning on January 1, 2015, and continuing through and including January 1, 2023, by 4% of the total number of shares of the Company's capital stock outstanding on December 31 of the preceding calendar year, or a lesser number of shares determined by the board of directors. The maximum number of shares that may be issued upon the exercise of ISOs under the 2013 Plan is 4,684,989 shares.

On September 11, 2017, the Company's compensation committee approved an amendment to the 2013 Plan to reserve an additional 1,500,000 of the Company's common stock to be used exclusively for grants of inducement awards to individuals who were not previously employees or non-employee directors of the Company (or following a bona fide period of non-employment with the Company).

As of December 31, 2020, 3,167,974 shares were available for future issuance under the 2013 Plan. As of December 31, 2020, there were 204,188 options outstanding under the 2009 Plan and 4,387,919 options outstanding under the 2013 Plan, including 623,565 shares underlying outstanding stock options granted as inducement awards under the 2013 Plan.

Employee Stock Purchase Plan

On January 27, 2014, the Company's stockholders approved the Employee Stock Purchase Plan. A total of 209,102 shares of common stock were reserved for issuance under this plan. The Employee Stock Purchase Plan became effective on February 11, 2014, the date of execution of the underwriting agreement pursuant to which the Company's common stock was priced for its initial public offering. During the years ended December 31, 2020 and 2019, 155,039and 184,860 shares, respectively, were purchased by employees under the plan. Additionally, the number of shares of common stock reserved for issuance under the Employee Stock Purchase Plan automatically increases on January 1 of each year, beginning on January 1, 2015, and continuing through and including January 1, 2023, by a number equal to the least of (a) 1% of the total number of shares of the Company's capital stock outstanding on December 31 of the preceding calendar year, (b) 375,768 shares of the Company's common stock; and (c) or a lesser number of shares determined by the board of directors.

13. Stock-Based Compensation

Stock Options

During the years ended December 31, 2020, 2019, and 2018, the Company granted stock options for the purchase of 452,000, 1,099,450, and 1,127,263 shares of common stock, respectively, to certain employees, two non-employees and directors. The vesting conditions for most of these awards are time-based, and the awards vest 25% after one year and monthly thereafter for the next 36 months, except for annual option grants to non-employee directors of the Company whose initial grants vest 25% after one year and monthly thereafter for the next 24 months and whose annual grants vest in equal monthly installments during the 12-month period following the grant date, pursuant to the Company's Non-Employee Director Compensation Policy. Options granted have a maximum term of up to 10 years.

Stock Option Valuation

The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option-pricing model. Expected volatility is based on historical volatility of the Company's common stock. The expected term of the Company's stock options has been determined utilizing the "simplified" method for awards that qualify as "plain vanilla" options. The expected term of stock options granted to non-employees is equal to the contractual term of the option award. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. Expected dividend yield is based on the fact that the Company has never paid cash dividends and does not expect to pay any cash dividends in the foreseeable future. The relevant data used to determine the value of the stock option grants for the years ended December 31, 2020, 2019, and 2018, is as follows:

	December 31,		
	2020	2019	2018
Risk-free interest rates	0.47% - 1.79%	1.42% - 2.67%	2.67% - 3.06%
Expected dividend yield	0.00%	0.00%	0.00%
Expected term (in years)	6.0	6.0	6.0
Expected volatility	65.4% - 72.5%	66.2% - 69.5%	69.8% - 75.3%

The following table summarizes stock option activity for the year ended December 31, 2020:

(In thousands, except per share amounts)	Shares Issuable Under Options		Weighted Average Exercise Price
Outstanding as of December 31, 2019	4,775	$	17.99
Granted	452	$	14.80
Exercised	(53)	$	6.27
Cancelled	(582)	$	18.34
Outstanding as of December 31, 2020	4,592	$	17.77
Options vested and expected to vest at December 31, 2020	4,592	$	17.77
Options exercisable at December 31, 2020	3,502	$	18.15

The aggregate intrinsic value of options is calculated as the difference between the exercise price of the options and the fair value of the Company's common stock for those options that had exercise prices lower than the fair value of the Company's common stock. A total of 53,429, 153,754, and 165,684 options were exercised during the years ended December 31, 2020, 2019, and 2018, respectively. The aggregate intrinsic value of stock options exercised was $0.3 million, $0.9 million, and $2.3 million for the years ended December 31, 2020, 2019, and 2018, respectively.

At December 31, 2020, 2019, and 2018, the Company had options for the purchase of 4,592,107, 4,774,691, and 4,435,056 shares of common stock outstanding, with a weighted average remaining contractual term of 6.3, 6.9, and 7.6 years, respectively, and with a weighted average exercise price of $17.77, $17.99, and $19.21 per share, respectively. At December 31, 2020, 2019, and 2018, there were options for the purchase of 3,501,905, 2,973,000, and 2,368,955 shares of common stock exercisable under these stock option awards, with a weighted average remaining contractual life of 5.7, 6.1, and 6.6 years, respectively, and an aggregate intrinsic value of $1.9 million, $9.8 million, and $2.6 million, respectively.

The weighted average grant date fair value of options granted during the years ended December 31, 2020, 2019, and 2018, was $8.86, $8.55, and $15.12, respectively.

Restricted Stock Units

During the year ended December 31, 2020, the Company awarded 1,835,042 RSUs to employees at an average grant date fair value of $13.73 per share, including 721,985 RSUs granted to substantially all of the Company's employees, including executive officers on July 16, 2020. RSUs granted to employees typically vest in four substantially equal installments on each of the first four anniversaries of the vesting commencement date, subject to the employee's continued employment with, or services to, the Company on each vesting date. The July 2020 RSUs granted to the Company's executive officers vest in equal annual installments over a 3-year vesting period, while the July 2020 RSUs granted to the Company's non-executive employees vest 1/3rd on the first anniversary of the grant date and 2/3rds on the second-year anniversary of the grant date. Compensation expense on RSUs is recognized on a straight-line basis.

Included in the 2020 RSU awards was a grant of 175,000 RSUs to the Company's chief executive officer. These RSUs had a performance condition in that they would only vest if the Company reaches a certain revenue threshold for the year ending December 31, 2020. If the threshold is reached, the RSUs vest in four substantially equal installments on each of the first four anniversaries of the vesting commencement date, subject to the employee's continued employment with, or services to, the Company on each vesting date. This award was modified on July 16, 2020, to take into account the impact of COVID-19 on the Company's projected revenues. The modification changed the revenue thresholds and the portion of the RSUs that vest based on achieving the new thresholds. As a result of the modification, the Company concluded that it was probable that the performance condition would be met for at least a portion of the RSUs granted. Therefore, the Company recognized $0.4 million of expense on these awards during the year ended December 31, 2020. The remaining expense will be recognized over the remaining vesting term.

The following table summarizes the RSU activity for the year ended December 31, 2020:

(In thousands, except per share amounts)	Number of Shares	Weighted Average Grant Date Fair Value Per Share
Nonvested balance as of December 31, 2019	853	$ 15.84
Granted	1,835	13.73
Cancelled	(275)	14.87
Vested/Released	(220)	16.29
Nonvested balance as of December 31, 2020	2,193	$ 14.15

Stock-based Compensation

The Company recorded stock-based compensation expense related to stock options, restricted stock and shares purchased under the Employee Stock Purchase Plan for the years ended December 31, 2020, 2019, and 2018, as follows:

	Year Ended December 31,		
(In thousands)	2020	2019	2018
Research and development	$ 6,346	$ 5,211	$ 4,728
Selling, general and administrative	12,231	10,690	10,731
Total	$ 18,577	$ 15,901	$ 15,459

As of December 31, 2020, unrecognized stock-based compensation expense for stock options outstanding was $10.2 million which is expected to be recognized over a weighted average period of 2.1 years. As of December 31, 2020, unrecognized stock-based compensation expense for RSUs outstanding was $23.1 million which is expected to be recognized over a period of 2.4 years.

14. Commitments and Contingencies

Operating Leases

Burlington Lease

In May 2013, the Company entered into a lease for office space in Burlington, Massachusetts (the “Lease”) for an initial term of 42 months. In July 2015, the Company amended the Lease to add additional square feet of office space and extend the term of the Lease through October 31, 2019. On April 7, 2017, the Company further amended the Lease to add additional square feet of office space and extend the term to October 31, 2023.

Upon adoption of ASU 2016-02, the Company recorded a right-of-use asset and corresponding lease liability for the Lease on January 1, 2019, by calculating the present value of lease payments, discounted at 8.9%, the Company’s estimated incremental borrowing rate, over the remaining term of the Lease.

In June 2019, the Company amended the Lease to add additional square feet of office space and extend the term of the Lease through April 30, 2025 (the “Amended Lease”). As a result of the Amended Lease, the total rentable floor area is 41,873 square feet. Starting in August 2019, the Company’s minimum monthly lease payment is approximately $108,000. which increases over the term of the Amended Lease. In addition to the base rent for the office space, the Company is responsible for its share of operating expenses and real estate taxes. The lease commencement date for the additional space, which represents the date the Company first had access to the space, was July 1, 2019. The Company accounted for the Amended Lease as a lease modification that is a separate contract from the original lease and recorded an incremental right-of-use asset and lease liability of $2.5 million, which represents the present value of the lease payments relating to the new space, as well as the lease payments relating to the 18-month extension of the existing space, as of the modification date, discounted at 6.8%.

The straight-line lease cost for the Amended Lease (including the expense relating to the original Lease) amounted to $1.9 million for the year ended December 31, 2020, respectively, and was included in operating expenses. As of December 31, 2020, the remaining lease term on the Amended Lease was 4.3 years, which includes the 18-month extension resulting from the amendment signed in June 2019.

Woburn Lease

In February 2017, the Company entered into a five-year lease for laboratory space located in Woburn, Massachusetts with a monthly lease payment of approximately $15,000, which increases over the term of the lease, plus a share of operating expenses.

Upon adoption of ASU 2016-02, the Company recorded a right-of-use asset and corresponding lease liability for the Lease on January 1, 2019, by calculating the present value of lease payments, discounted at 8.4%, the Company’s estimated

incremental borrowing rate, over the remaining term. The Woburn lease includes an option to extend the term of the lease for two years. Since the Company adopted ASU 2016-02 using the Comparatives under 840 approach, it did not reassess the determination of its operating leases as leases, and therefore no options to extend the lease were included in the calculation of the lease liability as of December 31, 2020. The straight-line lease cost for the Woburn lease amounted to $0.2 million for the year ended December 31, 2020, respectively, and was included in operating expenses. As of December 31, 2020, the remaining lease term on the Woburn lease was 1.2 years.

The Company incurred operating lease costs of $2.1 million, $2.0 million, and $1.1 million for the years ended December 31, 2020, 2019, and 2018, respectively.

Manufacturing and Supply Agreement with Patheon U.K. Limited

In July 2015, the Company and Patheon U.K. Limited ("Patheon") entered into a Manufacturing and Supply Agreement (the "Manufacturing Agreement") and Technical Transfer and Service Agreement (the "Technical Transfer Agreement") for the manufacture of ZILRETTA.

Patheon agreed in the Technical Transfer Agreement to undertake certain transfer activities and construction services needed to prepare Patheon's United Kingdom facility for the commercial manufacture of ZILRETTA in dedicated manufacturing suites. The Company provided Patheon with certain equipment and materials necessary to manufacture ZILRETTA and pays Patheon a monthly fee for such activities and reimburses Patheon for certain material, equipment and miscellaneous expenses and additional services.

The initial term of the Manufacturing Agreement is 10 years from approval by the FDA of the Patheon manufacturing suites for ZILRETTA, or until October 6, 2027. The Company pays a monthly base fee to Patheon for the operation of the manufacturing suites and a per product fee for each vial based upon a forecast of commercial demand. The Company also reimburses Patheon for purchases of materials and equipment made on its behalf, certain nominal expenses and additional services. The Manufacturing Agreement will remain in full effect unless and until it expires or is terminated. Upon termination of the Manufacturing Agreement (other than termination by Flexion in the event that Patheon does not meet the construction and manufacturing milestones or for a breach by Patheon), Flexion will be obligated to pay for the costs incurred by Patheon associated with the removal of our manufacturing equipment and for Patheon's termination costs up to a capped amount.

The Manufacturing Agreement with Patheon contains an operating lease for the use of dedicated manufacturing suites. With the adoption of ASU 2016-02, the Company recorded a right-of-use asset and corresponding lease liability for the operating lease.

In June 2019, the Company and Patheon amended the Manufacturing Agreement and the Technical Transfer Agreement. The amendment primarily modifies the compensation structure, which is comprised of base fees and per product fees the Company pays to Patheon and does not result in any additional rights of use. The Company accounted for the amendment as a lease modification that is not a separate contract from the original lease. As part of the modification, the Company reassessed whether the contract is or contains a lease and determined that there is an operating lease component for the use of dedicated manufacturing suites. The remainder of the consideration is allocated to the service component. The Company also reassessed the lease liability by calculating the present value of the remaining lease payments as of the modification date, discounted at 6.1%. The modification resulted in an increase to each of the lease liability and right of use asset of $0.5 million.

In April 2020, the Company entered into a side letter amending the Manufacturing Agreement with Patheon pursuant to which the parties agreed that the Company would continue to pay the monthly base fee for maintaining the manufacturing suites, but minimum purchase obligations would be cancelled for 2020 as the Company temporarily suspended manufacturing activities for ZILRETTA. In June 2020, the Company informed Patheon of its intent to restart manufacturing in the fourth quarter. The amendment did not change the amount of fixed consideration owed to Patheon over the life of the contract, nor did it grant the Company any additional rights of use. As such, there was no change in the accounting for the embedded lease as a result of this amendment.

As of December 31, 2020, the remaining lease term on the Patheon lease was 6.8 years. The straight-line lease cost amounted to $0.2 million for the year ended December 31, 2020, respectively, and is included in inventory as part of manufacturing overhead.

The components of lease expense and related cash flows were as follows:

(In thousands)	Year ended December 31, 2020	
Operating lease cost	**2020**	**2019**
Operating lease cost included in operating expenses	$ 2,054	$ 1,765
Operating lease cost included in inventory	230	204
Total operating lease cost	2,284	1,969
Operating cash flows from operating leases	2,958	2,363

Maturities of lease liability due under these lease agreements as of December 31, 2020, were as follows:

Year	**Aggregate Minimum Payments (in thousands)**
2021	2,043
2022	1,886
2023	1,894
2024	1,936
2025	813
Thereafter	428
Present value imputed interest	(2,331)
Present value of lease payments	$ 6,669

Other Commitments and Contingencies

Evonik Supply Agreement

In November 2016, the Company entered into a Supply Agreement with Evonik Corporation (“Evonik”) for the purchase of PLGA which is used in the manufacturing of potential clinical and commercial supply of ZILRETTA. Pursuant to the Supply Agreement, Flexion is obligated to submit rolling monthly forecasts to Evonik for PLGA supply, a portion of which will constitute binding orders. In addition, Flexion agreed to certain minimum purchase requirements and which do not apply (i) during periods in which Evonik is in material breach of the Supply Agreement or is unable to perform its obligations due to a force majeure event, (ii) with respect to orders that Evonik is unable to supply in excess of binding orders, (iii) for orders Evonik is unable to timely deliver or does not deliver conforming product and provides a credit for such order, or (iv) during an uncured material quality failure by Evonik. Flexion agreed to purchase PLGA batches at a specified price per gram in U.S. dollars, subject to adjustment from time to time, including due to changes in price indices and in the event the initial term of the Supply Agreement is extended. The total term of the agreement is five years. Upon termination of the Supply Agreement (other than termination due to the expiration of the term of the agreement or due to bankruptcy of either Evonik or Flexion), Flexion is obligated to pay the costs associated with the binding supply forecast provided to Evonik. The Supply Agreement will renew for two successive two-year terms upon mutual written consent by both parties.

Southwest Research Institute License Agreement

On July 25, 2014, the Company entered into an exclusive worldwide license agreement with Southwest Research Institute (“SwRI”) with respect to the use of SwRI’s proprietary microsphere manufacturing technologies for certain steroids formulated with PLGA, including ZILRETTA. Under the agreement, the Company paid an upfront fee of $120,000 to SwRI. In February 2017, Flexion executed an agreement with SwRI to transfer manufacturing equipment to SwRI in consideration for SwRI deeming the additional milestone payment to have been fully paid by Flexion.

FX201-Related Agreements

In December 2017, the Company entered into a definitive agreement with GeneQuine to acquire the global rights to FX201. As part of the asset purchase transaction with GeneQuine, the Company made an upfront payment to GeneQuine of $2.0 million. In 2018, the Company paid GeneQuine $750,000 for initiating a GLP toxicology study of FX201. In addition, the Company paid GeneQuine $750,000 in November 2019 following the FDA acceptance of the IND application for FX201. The next milestone of $2.5 million was achieved in March 2020 when the first patient was treated in the Phase 1 clinical trial. This milestone was recognized as research and development expense in the first quarter of 2020. The Company may also be required to make additional milestone payments during the development of FX201, including up to $4.5 million through initiation of the Phase 2 PoC, clinical trial and, following successful PoC, up to an additional $51.5 million in development and global regulatory approval milestone payments. The transaction was accounted for as an asset acquisition, as it did not qualify as a business combination. The upfront fee was attributed to the intellectual property acquired and recognized as

research and development expense in December 2017 as the FX201 rights had not been commercially approved and have no alternative future use. Milestone payments earned prior to regulatory approval of FX201 are recognized as research and development expense in the period when the milestone events become probable of being achieved. Future milestones earned upon regulatory approval would be recognized as an intangible asset and amortized to expense over its estimated life. As of December 31, 2020, no other milestones under the arrangement were probable of being achieved. As part of the transaction, the Company became the direct licensee of certain underlying Baylor College of Medicine (Baylor) patents and other proprietary rights related to FX201 for human applications. The Baylor license agreement grants the Company an exclusive, royalty-bearing, world-wide right and license (with a right to sublicense) for human applications under its patent and other proprietary rights directly related to FX201, with a similar non-exclusive license to certain Baylor intellectual property rights that are not specific to FX201. The license agreement with Baylor includes a low single-digit royalty on net sales of FX201 and requires the Company to use reasonable efforts to develop FX201 according to timelines set out in the license agreement. In December 2017, the Company also entered into a Master Production Services Agreement with SAFC Carlsbad, Inc., a part of MilliporeSigma, for the manufacturing of preclinical and initial clinical supplies of FX201. In addition, in February 2020 the Company entered into a manufacturing agreement with another vendor for clinical trial supply of FX201 through Phase 3 clinical trials.

FX301-Related Agreements

In September 2019, the Company entered into a definitive agreement with Xenon that provides the Company with the global rights to develop and commercialize XEN402, Xenon's NaV1.7 inhibitor known as funapide, formulated for extended release with a novel, Flexion proprietary thermosensitive hydrogel under the Company's preclinical program known as FX301. As part of the asset purchase transaction with Xenon, the Company made an upfront payment to Xenon of $3.0 million. The upfront fee was attributed to the intellectual property acquired and was recognized as research and development expense in September 2019 as the FX301 product candidate had not been commercially approved and had no alternative future use. The next milestone of $0.5 million was achieved following the commencement of the GLP toxicology study. This milestone was recognized as research and development expense in the first quarter of 2020. The Company may also be required to make additional milestone payments during the development of FX301, including up to $8.0 million through initiation of a Phase 2 clinical trial and, following the Phase 2 trial, up to $40.8 million in development and global regulatory approval milestone payments and up to an additional $75.0 million in sales-related milestone payments. Future milestone payments earned prior to the regulatory approval of FX301 would be recognized as research and development expense in the period when the milestone events become probable of being achieved. Future milestones earned subsequent to regulatory approval would be recognized as an intangible asset and amortized to expense over the estimated life of FX301. As of December 31, 2020, no other milestones under the arrangement were probable of being achieved. In February 2021, the FDA cleared the IND application for FX301, which triggered a milestone payment of $1.0 million. As part of the transaction, the Company became the direct licensee of certain underlying Xenon patents and other proprietary rights related to XEN402 for human applications. The Xenon agreement grants the Company an exclusive, royalty-bearing, world-wide right and license (with a right to sublicense) for human applications under its patents directly related to XEN402, with a similar royalty-free license to other Xenon proprietary rights directly related to XEN402. The agreement with Xenon includes a tiered royalty ranging from mid-single digits to low double digits that is based on aggregate annual net sales of FX301 and requires the Company to use reasonable efforts to develop FX301 according to timelines set out in the agreement.

15. Net Loss Per Share

Basic and diluted net loss per share attributable to common stockholders was calculated as follows for the years ended December 31, 2020, 2019, and 2018:

	Year ended December 31,		
(In thousands)	**2020**	**2019**	**2018**
Numerator:			
Net loss	$ (113,706)	$ (149,773)	$ (169,659)
Net loss:	$ (113,706)	$ (149,773)	$ (169,659)
Denominator:			
Weighted average common shares outstanding, basic and diluted	45,013	38,086	37,751
Net loss per share, basic and diluted	$ (2.53)	$ (3.93)	$ (4.49)

The following common stock equivalents were excluded from the calculation of diluted net loss per share as including them would have an anti-dilutive effect:

	Year ended December 31,		
	2020	**2019**	**2018**
Shares issuable upon conversion of the 2024 convertible notes	7,515	7,515	7,515

Stock Options	4,918	4,988	4,498
Restricted Stock Units	1,667	802	266
	14,100	13,305	12,279

16. Income Taxes

The Company recorded an income tax provision in the amount of $0.5 million for the year ended December 31, 2020, related to withholding taxes on the upfront payment received from the HK Tainuo license agreement. The Company did not record an income tax provision or benefit for the years ended December 31, 2019, and 2018, respectively.

A reconciliation of the U.S. federal statutory income tax rate to the Company's effective income tax rate is as follows:

	Year Ended December 31,		
	2020	2019	2018
Federal statutory income tax rate	21.0%	21.0%	21.0%
State taxes, net of federal benefit	7.0	(0.2)	8.0
Federal and state research and development tax credits	3.1	1.0	1.0
Change in deferred tax asset valuation allowance	(28.9)	(22.2)	(27.4)
Tax rate change	(1.0)	1.7	(1.9)
Other	(1.2)	(1.3)	(0.7)
Foreign withholding tax	(0.4)	0.0	0.0
Effective income tax rate	(0.4)%	—%	—%

The Company's net deferred tax assets consisted of the following:

	December 31,	
	2020	2019
Net operating loss carryforwards	$ 112,700	$ 101,356
Research and development tax credit carryforwards	16,291	12,096
Accruals and other temporary differences	8,908	1,772
Debt discount	(9,225)	(11,156)
Right of use asset	(1,678)	(2,042)
Stock-based compensation	9,275	6,876
Lease liability	1,951	2,225
Capitalized research and development expenses, net	49,107	43,442
Total deferred tax assets	187,329	154,569
Valuation allowance	(187,329)	(154,569)
Net deferred tax asset	$ —	$ —

As of December 31, 2020, the Company had federal and state net operating loss ("NOL") carryforwards of approximately $448.2 million and $340.1 million, respectively, which begin to expire in 2029 for federal purposes and in 2030 for state purposes. Approximately $258.7 million of the federal NOLs have an indefinite carryforward. In addition, the Company had federal and state research and development tax credit carryforwards of approximately $12.2 million and $5.2 million, respectively, available to reduce future tax liabilities, which begin to expire in 2029 for federal purposes and 2025 for state purposes. Management of the Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets, which are comprised principally of NOL carryforwards and capitalized research and development expenses. Management has considered the Company's history of cumulative net losses incurred since inception and determined that it is more likely than not that the Company will not realize the benefits of its deferred tax assets. As a result, a full valuation allowance has been established at December 31, 2020, 2019, and 2018.

Section 382 of the Internal Revenue Code of 1986, as amended ("Section 382"), contains rules that limit the ability of a company that undergoes an ownership change to utilize its NOLs, and tax credits existing as of the date of such ownership change. Under the rules, such an ownership change is generally any change in ownership of more than 50% of a company's stock within a rolling three-year period. The rules generally operate by focusing on changes in ownership among stockholders considered by the rules as owning, directly or indirectly, 5% or more of the stock of a company and any change in ownership arising from new issuances of stock by the company. The Company has experienced multiple ownership changes since its inception, however, based on the annual limitations calculated at each ownership change date, substantially all NOL carryforwards will be available to offset future taxable income. Future ownership changes as defined by Section 382 may further limit the amount of NOL carryforwards that could be utilized annually to offset future taxable income.

Changes in the valuation allowance for deferred tax assets during the years ended December 31, 2020, 2019, and 2018, were as follows:

	Year Ended December 31,		
	2020	2019	2018
Valuation allowance as of beginning of year	$ (154,569)	$ (121,379)	$ (74,842)
Decreases recorded as benefit to income tax provision	0	2,046	1,913
Decreases recorded as benefit to equity	0	0	0
Increases recorded to income tax provision	(32,760)	(35,236)	(48,450)
Valuation allowance as of end of year	$ (187,329)	$ (154,569)	$ (121,379)

In each reporting period, the Company considers whether a tax position of the Company is more likely than not to be sustained upon examination, including resolution of any related appeals of litigation processes, based on the technical merits of the position. For tax positions meeting the more likely than not threshold, the tax amount recognized in the financial statements is reduced by the largest benefit that has a greater than fifty percent likelihood of being realized upon the ultimate settlement with the relevant taxing authority. No liabilities for unrecognized tax benefits were recorded as of as of December 31, 2020 and 2019.

The Company files tax returns as prescribed by the tax laws of the jurisdictions in which it operates. In the normal course of business, the Company is subject to examination by federal and state jurisdictions, where applicable. There are currently no pending tax examinations. The Company's tax years are still open under statute from 2013 to the present. Earlier years may be examined to the extent that tax credit or NOL carryforwards are used in future periods. The resolution of tax matters is not expected to have a material effect on the Company's consolidated financial statements.

17. Quarterly Financial Data (unaudited)

The following information has been derived from unaudited consolidated financial statements that, in the opinion of management, include all recurring adjustments necessary for a fair statement of such information.

	Three Months Ended			
(in thousands, except per share amounts)	March 31, 2020	June 30, 2020	September 30, 2020	December 31, 2020
Revenues	$ 20,127	$ 15,451	$ 23,664	$ 26,310
Gross profit	17,851	9,970	18,534	19,948
Net loss	(36,802)	(32,619)	(24,638)	(19,647)
Net loss per common share—basic and diluted	$ (0.95)	$ (0.76)	$ (0.50)	$ (0.40)
Weighted average common shares—basic and diluted	38,553	42,776	49,298	49,331

	Three Months Ended			
(in thousands, except per share amounts)	March 31, 2019	June 30, 2019	September 30, 2019	December 31, 2019
Revenues	$ 10,564	$ 16,953	$ 21,786	$ 23,653
Gross profit	8,802	15,555	18,914	19,725
Net loss	(41,538)	(36,487)	(38,232)	(33,516)
Net loss per common share—basic and diluted	$ (1.09)	$ (0.96)	$ (1.00)	$ (0.88)
Weighted average common shares—basic and diluted	37,992	38,010	38,125	38,176

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

We are responsible for maintaining disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act. Disclosure controls and procedures are controls and other procedures designed to ensure that the information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by us in the reports that we file or submit under the Exchange Act 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.

Based on our management's evaluation (with the participation of our principal executive officer and our principal financial officer) of our disclosure controls and procedures as defined by Rule 13a-15(e) and Rule 15d-15(e) under the Exchange Act, our principal executive officer and our principal financial officer have concluded that our disclosure controls and procedures were effective to achieve their stated purpose as of December 31, 2020, the end of the period covered by this report.

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as such term is defined in Exchange Act Rule 13a-15(f) and Exchange Act Rule 15d-15(f). 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 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.

As of December 31, 2020, 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, as of December 31, 2020, our internal control over financial reporting was effective based on those criteria.

This annual report does not include an attestation report of our registered public accounting firm as we are considered a non-accelerated filer and a smaller reporting company under the amended guidelines set forth in Rule 12b-2 of the Exchange Act. The amendments were effective April 27, 2020, and apply to an annual report filing due on or after the effective date.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting during the quarter ended December 31, 2020, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

The information required by this item and not set forth below will be set forth in the section headed “Election of Directors” and “Executive Officers” in our Proxy Statement for our 2021 Annual Meeting of Stockholders, or Proxy Statement, to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2020, and is incorporated herein by reference.

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. A current copy of the code is available on the Corporate Governance section of our website, www.flexiontherapeutics.com. We intend to disclose on our website any amendments to, or waivers from, our code of business conduct and ethics that are required to be disclosed pursuant to SEC rules.

Section 16(a) Compliance

The information concerning Section 16(a) beneficial ownership reporting compliance will be set forth in the section headed “Delinquent Section 16(a) Reports” in our Proxy Statement and is incorporated herein by reference.

Item 11. Executive Compensation

The information required by this item will be set forth in the section headed “Executive Compensation” in our Proxy Statement and is incorporated herein by reference.

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

The information required by this item will be set forth in the section headed “Security Ownership of Certain Beneficial Owners and Management” in our Proxy Statement and is incorporated herein by reference.

The information required by Item 201(d) of Regulation S-K will be set forth in the section headed “Executive Compensation” in our Proxy Statement and is incorporated herein by reference.

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

The information required by this item will be set forth in the section headed “Transactions With Related Persons” in our Proxy Statement and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services

The information required by this item will be set forth in the section headed “Ratification of Selection of Independent Registered Public Accounting Firm” in our Proxy Statement and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules

(a) Documents filed as part of this report.

1. Financial Statements

The financial statements of Flexion Therapeutics, Inc. listed below are set forth in Item 8 of this report for the year ended December 31, 2020:

2. Financial Statement Schedules

These schedules have been omitted because the required information is included in the consolidated financial statements or notes thereto or because they are not applicable or not required.

3. Exhibits

Unless otherwise indicated, all references to previously filed exhibits refer to Flexion's filings with the SEC under File No. 001-36287. The following exhibits are filed as part of, or incorporated by reference, into this report. Each management contract or compensatory plan or arrangement required to be identified by this item is so designated in such list.

Exhibit Number	Description
3.1	Amended and Restated Certificate of Incorporation of Flexion (Exhibit 3.1, Current Report on Form 8-K filed on February 19, 2014)
3.2	Amended and Restated Bylaws of Flexion (Exhibit 3.2, Current Report on Form 8-K filed on February 19, 2014)
4.1	Form of Common Stock Certificate of Flexion (Exhibit 4.1, Registration Statement on Form S-1 (File No. 333-193233), as amended, filed on January 29, 2014)
4.2	Indenture, dated as of May 2, 2017, by and between Flexion and Wells Fargo Bank, National Association, as trustee (Exhibit 4.1, Current Report on Form 8-K filed on May 2, 2017)
4.3	Form of Note representing Flexion's 3.375% Convertible Senior Notes due 2024 (included as Exhibit A to the Indenture filed as Exhibit 4.1, Current Report on Form 8-K filed on May 2, 2017)
4.4	Consent and Second Amendment to Credit and Security Agreement, dated April 24, 2017, between Flexion and MidCap Financial Trust, as administrative agent (Exhibit 4.3, Current Report on Form 8-K filed on May 2, 2017)
4.5	Description of Common Stock (Exhibit 4.5, Annual Report on Form 10-K filed on March 12, 2020)
	Management Contracts and Compensatory Plans
10.1	Form of Indemnity Agreement between Flexion and its directors and officers (Exhibit 10.1, Registration Statement on Form S-1 (File No. 333-193233) filed on January 8, 2014)
10.2	Flexion Therapeutics, Inc. 2009 Equity Incentive Plan and Forms of Stock Option Agreement, Notice of Exercise and Stock Option Grant Notice thereunder (Exhibit 10.2, Registration Statement on Form S-1 (File No. 333-193233) filed on January 8, 2014)
10.3	Flexion Therapeutics, Inc. 2013 Equity Incentive Plan, as amended, and Forms of Stock Option Agreement, Notice of Exercise and Stock Option Grant Notice thereunder (Exhibit 99.1, Current Report on Form 8-K, filed September 14, 2017)

Exhibit Number	Description
10.4	Form of Restricted Stock Unit Award Agreement and Restricted Stock Unit Grant Notice under the Flexion Therapeutics, Inc. 2013 Equity Incentive Plan (Exhibit 99.1, Current Report on Form 8-K filed on December 22, 2015)
10.5	Flexion Therapeutics, Inc. 2013 Employee Stock Purchase Plan (Exhibit 10.4, Registration Statement on Form S-1 (File No. 333-193233), as amended, filed on January 29, 2014)
10.6	Flexion Therapeutics, Inc. Non-Employee Director Compensation Policy, as revised (Exhibit 10.6, Annual Report on Form 10-K filed on March 12, 2020)
10.7	Amended and Restated Offer Letter between Flexion and Michael D. Clayman, M.D. (Exhibit 10.6, Registration Statement on Form S-1 (File No. 333-193233) filed on January 8, 2014)
10.8	Amendment to Amended and Restated Offer Letter between Flexion and Michael D. Clayman, M.D. (Exhibit 10.7, Annual Report on Form 10-K filed on March 28, 2014)
10.9	Amended and Restated Offer Letter between Flexion and Scott Kelley, M.D. (Exhibit 10.11, Annual Report on Form 10-K filed on March 8, 2018)
10.10	Amended and Restated Offer Letter between Flexion and Mark Levine (Exhibit 10.12, Annual Report on Form 10-K filed on March 8, 2018)
10.11	Amended and Restated Offer Letter between Flexion and Kerry Wentworth (Exhibit 10.13, Annual Report on Form 10-K filed on March 8, 2018)
10.12	Offer Letter between Flexion and David Arkowitz (Exhibit 10.1, Quarterly Report on Form 10-Q filed on May 8, 2018)
10.13	Amended and Restated Offer Letter between Flexion and Christina Willwerth (Exhibit 10.15, Annual Report on Form 10-K filed on February 28, 2019)
10.14	Flexion Therapeutics, Inc. Change in Control Severance Benefit Plan and Form of Participation Agreement (Exhibit 99.1, Current Report on Form 8-K filed on June 23, 2017)
10.15	Separation and Consulting Agreement between Flexion and Neil Bodick, dated December 9, 2019 (Exhibit 10.15, Annual Report on Form 10-K filed on March 12, 2020)
10.16	Offer Letter between Flexion and Melissa Layman (Exhibit 10.1, Quarterly Report on Form 10-Q filed on May 7, 2020)
10.17	Offer Letter between Flexion and Adam Muzikant dated January 1, 2021
	Other Agreements
10.18	Lease, dated February 22, 2013, between Flexion and The Trustees of Mall Road Trust (Exhibit 10.14, Registration Statement on Form S-1 (File No. 333-193233) filed on January 8, 2014)
10.19	First Amendment of Lease, dated July 13, 2015, between Flexion and CIP II/RJK 10-20 BMR Owner, LLC (as successor in interest to The Trustees of Mall Road Trust) (Exhibit 10.3, Quarterly Report on Form 10-Q filed on November 9, 2015)
10.20	Second Amendment of Lease, dated December 15, 2015, between Flexion and CIP II/RJK 10-20 BMR Owner, LLC (Exhibit 10.20, Annual Report on Form 10-K filed on March 11, 2016)
10.21*	Exclusive License Agreement, dated July 25, 2014, between Flexion and Southwest Research Institute (Exhibit 10.21, Annual Report on Form 10-K filed on March 11, 2016)
10.22*	Manufacturing and Supply Agreement, dated July 31, 2015, between Flexion and Patheon UK Limited (Exhibit 10.1, Quarterly Report on Form 10-Q filed on November 9, 2015)
10.23*	Technical Transfer and Service Agreement, dated July 31, 2015, between Flexion and Patheon UK Limited (Exhibit 10.2, Quarterly Report on Form 10-Q/A filed on January 26, 2016)
10.24	Amended and Restated Credit and Security Agreement, dated August 2, 2019, by and among Flexion, Silicon Valley Bank as agent, MidCap Financial Trust, Flexpoint MCLS Holdings, LLC and the other lenders from time to time party thereto (Exhibit 99.3, Current Report on Form 8-K filed on August 6, 2019)
10.25	Third Amendment of Lease, dated May 8, 2016, between Flexion and CIP II/RJK 10-20 BMR Owner, LLC (Exhibit 10.1, Quarterly Report on Form 10-Q filed on August 3, 2016)
10.26	Fourth Amendment of Lease, dated June 29, 2016, between Flexion and CIP II/RJK 10-20 BMR Owner, LLC (Exhibit 10.2, Quarterly Report on Form 10-Q filed August 3, 2016)
10.27	Fifth Amendment of Lease, dated July 21, 2016, between Flexion and CIP II/RJK 10-20 BMR Owner, LLC (Exhibit 10.3, Quarterly Report on Form 10-Q filed August 3, 2016
10.28	Sixth Amendment of Lease, dated September 21, 2016, between Flexion and CIP II/RJK 10-20 BMR Owner, LLC (Exhibit 10.1, Quarterly Report on Form 10-Q filed on November 7, 2016)

Exhibit Number	Description
10.29	Seventh Amendment of Lease, dated September 21, 2016, between Flexion and CIP II/RJK 10-20 BMR Owner, LLC (Exhibit 10.1, Quarterly Report on Form 10-Q filed on August 8, 2017)
10.30*	Supply Agreement, dated November 10, 2016, between Flexion and Evonik Corporation (Exhibit 10.29, Annual Report on Form 10-K filed on March 10, 2017)
10.31	Amendment to Exclusive License Agreement, dated February 7, 2017, between Flexion and Southwest Research Institute (Exhibit 10.30, Annual Report on Form 10-K filed on March 10, 2017)
10.32*	First Amendment to the Technical Transfer and Service Agreement, dated May 12, 2019, between Flexion and Patheon UK Limited (Exhibit 10.1, Quarterly Report on Form 10-Q filed on August 6, 2019)
10.33*	First Amendment to the Manufacturing and Supply Agreement, dated May 12, 2019, between Flexion and Patheon UK Limited (Exhibit 10.2, Quarterly Report on Form 10-Q filed on August 6, 2019)
10.34*	Second Amendment to the Manufacturing and Supply Agreement, dated June 21, 2019, between Flexion and Patheon UK Limited (Exhibit 10.3, Quarterly Report on Form 10-Q filed on August 6, 2019)
10.35	Eighth Amendment of Lease, dated June 21, 2019, between Flexion and CIP II/RJK 10-20 BMR Owner LLC (Exhibit 10.4, Quarterly Report on Form 10Q filed on August 6, 2019)
10.36*	Side Letter to the Patheon Manufacturing and Supply Agreement dated as of April 8, 2020 (Exhibit 10.2, Quarterly Report on Form 10-Q filed on May 7, 2020)
10.37	Amendment 1 to Amended and Restated Credit and Security Agreement dated as of May 18, 2020, by and among Flexion Therapeutics, Inc., Silicon Valley Bank as agent, MidCap Financial Trust, Flexpoint MCLS Holdings, LLC and the other lenders from time to time party thereto (Exhibit 99.1, Current Report on Form 8-K filed on May 19, 2020)
10.38	Equity Distribution Agreement dated November 4, 2020, by and among Flexion Therapeutics, Inc., Goldman Sachs & Co. LLC, and Credit Suisse Securities (USA) LLC (Exhibit 1.1, Current Report on Form 8-K filed November 4, 2020)
21.1	Subsidiaries of Flexion Therapeutics, Inc.
23.1	Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm
24.1	Power of Attorney (reference is made to the signature page thereto)
31.1	Certification of the Principal Executive Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934
31.2	Certification of the Principal Financial and Accounting Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934
32.1	Certification of Principal Executive Officer pursuant to Rule 13a-14(b) or 15d-14(b) of the Exchange Act and 18 U.S.C. Section 1350
32.2	Certification of Principal Financial and Accounting Officer pursuant to Rule 13a-14(b) or 15d-14(b) of the Exchange Act and 18 U.S.C. Section 1350
101.INS	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because XBRL tags are embedded within the Inline XBRL document.
101.SCH	Inline XBRL Taxonomy Extension Schema Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

* Pursuant to Item 601(b)(10) of Regulation S-K, certain portions of this exhibit have been omitted by means of marking such portions with asterisks because Flexion has determined that the information is not material and would likely cause competitive harm to Flexion if publicly disclosed.

Item 16. 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized on the 10th day of March, 2021.

FLEXION THERAPEUTICS, INC.

By: /s/ Michael D. Clayman, M.D.
Michael D. Clayman, M.D.
President and Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Michael D. Clayman, M.D. and Mark S. Levine, and each of them, his true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him and in his name, place and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments) to this report, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or either of them, or their or his substitutes or substitute, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Michael D. Clayman, M.D. Michael D. Clayman, M.D.	President, Chief Executive Officer and Member of the Board of Directors *(Principal Executive Officer)*	March 10, 2021
/s/ David Arkowitz David Arkowitz	Chief Financial Officer *(Principal Financial and Accounting Officer)*	March 10, 2021
/s/ Patrick J. Mahaffy Patrick J. Mahaffy	Chairman of the Board of Directors	March 10, 2021
/s/ Scott Canute Scott Canute	Member of the Board of Directors	March 10, 2021
/s/ Samuel D. Colella Samuel D. Colella	Member of the Board of Directors	March 10, 2021
/s/ Elizabeth Kwo, M.D. Elizabeth Kwo, M.D.	Member of the Board of Directors	March 10, 2021
/s/ Heath Lukatch, Ph.D. Heath Lukatch, Ph.D.	Member of the Board of Directors	March 10, 2021
/s/ Sandesh Mahatme Sandesh Mahatme	Member of the Board of Directors	March 10, 2021
/s/ Ann Merrifield Ann Merrifield	Member of the Board of Directors	March 10, 2021
/s/ Alan Milinazzo Alan Milinazzo	Member of the Board of Directors	March 10, 2021
/s/Mark Stejbach Mark Stejbach	Member of the Board of Directors	March 10, 2021

Flexion Therapeutics
10 Mall Road, Suite 301, Burlington MA 01803
www.flexiontherapeutics.com
info@flexiontherapeutics.com
781.305.7777

As of January 1, 2020

Adam Muzikant
[_____]
[_____]

Dear Adam:

We are pleased to offer you continued employment with Flexion Therapeutics, Inc. (the "Company"), as Chief Business Officer, reporting to Michael Clayman. This letter agreement (the "Agreement") replaces and supersedes the offer letter between you and the Company dated August 15, 2016 and as amended on July 25, 2017.

Compensation: Your compensation package includes the following:

- ***Salary.*** A base salary at the rate of $15,192.30 on a bi-weekly basis (which equates to $395,000 on an annualized basis), less payroll deductions and all required withholdings and payable in accordance with the Company's standard payroll practices as may be modified from time to time. As an exempt salaried employee, you are not eligible for overtime pay. You are eligible for performance reviews on a periodic basis and may be eligible for annual salary increases as long as you remain employed by Flexion.

- ***Bonus.*** Effective with the annual bonus payable in connection with the 2021 calendar year, a discretionary target performance bonus of forty-five percent (45%) of your base salary (which bonuses, if any, are calculated annually, and subject to approval by the Board of Directors of the Company (the "Board")). Among other eligibility factors for such a discretionary bonus to be determined by the Board, you must be employed in good standing at the time that bonuses are paid out in order to be eligible for such a bonus. Bonuses are paid on or before March 15th of the calendar year following the applicable "bonus" year.

- ***Change of Control Severance Benefits.*** You are eligible for benefits under the Company's Change in Control Severance Benefit Plan (the "CIC Plan") and Participation Agreement (the "Participation Agreement"), which is included with this Agreement.

Benefits: You will be eligible to participate on the same basis as similarly situated employees in the Company's benefit plans in effect from time to time during your employment. All matters of eligibility for coverage or employee benefits under any benefit plan shall be determined in accordance with the provisions of such plan. For a more detailed understanding of the Company's benefits and the eligibility requirements, please consult the policies and summary plan descriptions for the programs which will be made available to you. Please note that the Company reserves the right to change, alter, or terminate any benefit plan in its sole discretion.

At-Will Employment; Certain Conditions of Employment: Your employment with the Company is "at will," which means that the Company may modify the terms of employment at any time, and either you or the Company may terminate your employment at any time for any or no reason, with or without prior notice. Along these same lines, please note that nothing in this Agreement is a promise or guarantee of employment for any specific period of time or for continued employment.

In addition to the above, by signing this Agreement you are representing that you have full authority to accept this position and perform the duties of the position without conflict with any other obligations, and that you are not involved in any situation that might create, or appear to create, a conflict of interest with respect to your loyalty to

or duties for the Company. You specifically warrant that you are not subject to an employment agreement or restrictive covenant preventing full performance of your duties to the Company.

You further acknowledge that the Board has determined that you will be performing significant policy-making functions for the Company and shall therefore be regarded as a Section 16 officer of the Company pursuant to Section 16(a) of the Securities Exchange Act ("Section 16 Officer"). For so long as the Board continues to regard you as a Section 16 Officer, you acknowledge your obligation to make certain periodic filings with the SEC, including but not limited to, the "Initial Statement of Beneficial Ownership of Securities" on Form 3 and the "Statement of Changes of Beneficial Ownership of Securities" on SEC Form 4. You represent and warrant that you will timely comply with all obligations relating to your role as a Section 16 Officer.

Severance Eligibility: Subject to the other provisions of this Agreement, upon termination of your employment, the Company shall pay your base salary and accrued and unused vacation benefits earned through the date of termination at the rate in effect at the time of termination, less standard deductions and withholdings (the "Accrued Obligations"). In addition, you will be eligible for the following severance benefits if your employment is terminated under the circumstances described below.

If the Company terminates your employment without Cause (as defined below) or if you terminate your employment for Good Reason (as defined below) and provided such termination constitutes a "Separation from Service" (as defined under U.S. Treasury Regulation Section 1.409A-1(h), without regard to any alternative definition thereunder) and such termination is not as a result of your death or Disability, then in addition to the Accrued Obligations, you will be eligible to receive the following benefits:

(i) You shall continue to receive your then-current base salary (ignoring any decrease that forms the basis for your termination for Good Reason, if applicable), less standard deductions and withholdings, for fifteen (15) months following the date of termination (the "Severance Period").

(ii) If you are eligible for and timely elect to continue your health insurance coverage under the Company's group health plans under the Consolidated Omnibus Budget Reconciliation Act of 1985 or the state equivalent ("COBRA"), the Company will pay the COBRA premiums for you and your eligible dependents until the earlier of (A) the end of the Severance Period, (B) the expiration of your eligibility for the continuation coverage under COBRA or (C) such time as you become employed by another employer or self-employed through which you are eligible for health insurance (thereafter, you will be responsible for all COBRA premium payments, if any) (such period from your termination date through the earliest of (A) through (C), the "COBRA Payment Period"). For purposes of this Section, references to COBRA premiums shall not include any amounts payable by you under an Internal Revenue Code Section 125 health care reimbursement plan. Notwithstanding the foregoing, if the Company determines, in its sole discretion, that the Company cannot provide the COBRA premiums without potentially incurring financial costs or penalties under applicable law (including, without limitation, Section 2716 of the Public Health Service Act), the Company shall in lieu thereof pay you a taxable cash amount, which payment shall be made regardless of whether you elect health care continuation coverage (the "Health Care Benefit Payment"). The Health Care Benefit Payment shall be paid in monthly installments on the same schedule that the COBRA premiums would otherwise have been paid to you and shall be equal to the amount that the Company would have otherwise paid for COBRA premiums (which amount shall be calculated based on your COBRA premium for the first month of coverage), and shall be paid until the earlier of (i) expiration of the COBRA Payment Period or (ii) the date you voluntarily enroll in a health insurance plan offered by another employer or entity.

(iii) If your termination occurs within one (1) month prior to or twelve (12) months following a Change in Control, you shall be eligible to receive the payments and benefits as described in the Company's Change in Control Severance Benefit Plan (the "CIC Plan") and the Participation Agreement thereunder (the "Participation Agreement") attached thereto. If as a result of your termination or resignation you become entitled to severance benefits under the CIC Plan and you are also entitled to severance benefits described under Sections (i) and (ii) of the "Severance Eligibility" section of this Agreement above, the severance benefits under the CIC Plan shall be provided in lieu of the severance benefits you are entitled to under Sections (i) and (ii) of the "Severance Eligibility" section of this Agreement described above.

Severance benefits under this Agreement are expressly conditioned upon (a) your delivery to the Company of a signed release and waiver of claims in such form as may be specified by the Company (the **"**Release**"**) within the applicable deadline set forth therein, and permitting the Release to become effective in accordance with its terms no later than the Release Deadline (as defined in the Section 409A Section below); and (b) your fully complying with your obligations under your Proprietary Information, Inventions, Non-Solicitation, and Non-Competition Agreement dated July 25, 2017 which remains in full force and effect.

For the avoidance of doubt, you shall not be eligible for severance and continued benefits (other than the Accrued Obligations) if you resign without Good Reason, are terminated by the Company for Cause, or are terminated due to your death or Disability.

Definitions: For purposes of this Agreement, the following terms shall have the following meanings set forth in the CIC Plan: Cause, Good Reason, and Change in Control.

Section 409A: Notwithstanding anything in this Agreement to the contrary, the following provisions apply to the extent severance benefits provided herein are subject to Section 409A of the Internal Revenue Code of 1986, as amended (the "Code") and the regulations and other guidance thereunder and any state law of similar effect (collectively "Section 409A"). Severance benefits shall not commence until you have a Separation from Service. Each installment of severance benefits is a separate "payment" for purposes of Treasury Regulations Section 1.409A-2(b)(2)(i), and the severance benefits are intended to satisfy the exemptions from application of Section 409A provided under Treasury Regulations Sections 1.409A-1(b)(4), 1.409A-1(b)(5) and 1.409A-1(b)(9). However, if such exemptions are not available and you are, upon Separation from Service, a "specified employee" for purposes of Section 409A, then, solely to the extent necessary to avoid adverse personal tax consequences under Section 409A, the timing of the severance benefits payments shall be delayed until the earlier of (i) six (6) months and one day after your Separation from Service, or (ii) your death. You shall receive severance benefits only if you execute and return to the Company the Release within the applicable time period set forth therein and permit such Release to become effective in accordance with its terms, which date may not be later than sixty (60) days following the date of your Separation from Service (such latest permitted date, the "Release Deadline"). If the severance benefits are not covered by one or more exemptions from the application of Section 409A and the Release could become effective in the calendar year following the calendar year in which your Separation from Service occurs, the Release will not be deemed effective any earlier than the Release Deadline. None of the severance benefits will be paid or otherwise delivered prior to the effective date of the Release. Except to the minimum extent that payments must be delayed because you are a "specified employee" or until the effectiveness of the Release, all amounts will be paid as soon as practicable in accordance with the schedule provided herein and in accordance with the Company's normal payroll practices. All in-kind benefits provided and expenses eligible for reimbursement under this Agreement shall be provided by the Company or incurred by you during the time periods described in this Agreement. All reimbursements shall be paid as soon as administratively practicable, but in no event shall any reimbursement be paid after the last day of the taxable year following the taxable year in which the expense was incurred. The amount of in-kind benefits provided, or reimbursable expenses incurred in one taxable year shall not affect the in-kind benefits to be provided or the expenses eligible for reimbursement in any other taxable year. Such right to reimbursement or in-kind benefits is not subject to liquidation or exchange for another benefit. The benefits under this Agreement are intended to qualify for an exemption from application of Section 409A or comply with its requirements to the extent necessary to avoid adverse personal tax consequences under Section 409A, and any ambiguities herein shall be interpreted accordingly.

Compliance with Rules, etc.: You will comply at all times with (i) all Company policies, rules and procedures as they may be established, stated and/or modified from time to time at the Company's sole discretion, (ii) the terms of that certain Proprietary Information, Inventions, Non-Solicitation, and Non-Competition Agreement that you signed with the Company on August 4, 2017 and which remains in full force and effect, and (iii) all laws and regulations applicable to the Company's business and your performance of your duties for the Company.

General: By signing this Agreement, you acknowledge that the terms described in this letter, together with the Equity Documents and Proprietary Information Agreement attached hereto, set forth the entire offer to you and understanding between you and the Company and supersedes any prior representations or agreements, whether

written or oral pertaining to the subject matter herein. You further acknowledge that there are no terms, conditions, representations, warranties or covenants other than those contained herein. No term or provision of this letter may be amended waived, released, discharged or modified except in writing, signed by you and an authorized officer of the Company, except that the Company may, in its sole discretion, adjust salaries, incentive compensation, stock plans, benefits, job titles, locations, duties, responsibilities, and reporting relationships.

We look forward to your continued contributions to the Flexion team.

Sincerely,

/s/ Michael Clayman

Chief Executive Officer

ACCEPTED AND AGREED TO:

Name: /s/ Adam Muzikant Date: January 4, 2021

Adam Muzikant

Attachments: Change in Control Severance Benefit Plan Participation Agreement

Exhibit 21.1

Subsidiaries of Flexion Therapeutics, Inc.

NAME:	JURISDICTION OF INCORPORATION:
Flexion Therapeutics Securities Corporation	Massachusetts

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Form S-3 (No. 333-248749) and Form S-8 (Nos. 333-237132, 333-193907, 333-202957, 333-210111, 333-216615, 333-221373, 333-223532 and 333-229969) of Flexion Therapeutics, Inc. of our report dated March 10, 2021 relating to the financial statements, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP
Boston, Massachusetts
March 10, 2021

Exhibit 31.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER
PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Michael D. Clayman, M.D., certify that:

1. I have reviewed this Annual Report on Form 10-K of Flexion Therapeutics, Inc.;

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

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

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

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

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

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

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

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

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

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

Date: March 10, 2021

/s/ Michael D. Clayman, M.D.
Michael D. Clayman, M.D.
President and Chief Executive Officer

Exhibit 31.2

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER
PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, David A. Arkowitz, certify that:

1. I have reviewed this Annual Report on Form 10-K of Flexion Therapeutics, Inc.;

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

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

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

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

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

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

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

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

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

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

Date: March 10, 2021

/s/ David A. Arkowitz
David A. Arkowitz
Principal Financial and Accounting Officer

Exhibit 32.1

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

I, Michael D. Clayman, M.D., President and Chief Executive Officer of Flexion Therapeutics, Inc. (the "Registrant"), do hereby certify in accordance with 18 U.S.C. 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, based upon my knowledge:

(1) this Annual Report on Form 10-K of the Registrant, to which this certification is attached as an exhibit (the "Report"), fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934 (15 U.S.C. 78m); and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Registrant.

Date: March 10, 2021

/s/ Michael D. Clayman, M.D.
Michael D. Clayman, M.D.
President and Chief Executive Officer

The foregoing certification is being furnished solely pursuant to 18 U.S.C. Section 1350 and is not being filed as part of the Report or as a separate disclosure document.

Exhibit 32.2

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

I, David A. Arkowitz, Chief Financial Officer of Flexion Therapeutics, Inc. (the "Registrant"), do hereby certify in accordance with 18 U.S.C. 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, based upon my knowledge:

(1) this Annual Report on Form 10-K of the Registrant, to which this certification is attached as an exhibit (the "Report"), fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934 (15 U.S.C. 78m); and

(2) the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Registrant.

Date: March 10, 2021

/s/ David A. Arkowitz
David A. Arkowitz
Principal Financial and Accounting Officer

The foregoing certification is being furnished solely pursuant to 18 U.S.C. Section 1350 and is not being filed as part of the Report or as a separate disclosure document.