assembly bio

ANNUAL REPORT 2019

DEAR FELLOW SHAREHOLDERS,

When I was approached in 2019 with the opportunity to lead Assembly Biosciences, I was struck by the exceptional quality of the science, founders, and team, and the tremendous opportunity we have before us. For many years, I have believed in a future with new, curative treatment regimens for individuals with chronic Hepatitis B, of which there are nearly a quarter of a billion worldwide. I embraced this challenge and the opportunity to focus on such an important global problem, having undertaken a similar effort earlier in my career with Hepatitis C, which is fortunately now a curable disease.

I'm also pleased that over the course of the past year **we have been able to attract a number of highly experienced and talented leaders to augment our senior team. Like me, they recognized the opportunity for Assembly to bring novel, and potentially curative, treatments to patients.** Importantly, with the completion of our securities offering this past December, our team also has the financial resources needed to advance our programs, and we expect our current cash to fund operations into 2022.

OUR HEPATITIS B CORE INHIBITOR PORTFOLIO: DRIVING TOWARD CURE

Assembly's vision is to lead the advancement of curative, finite duration regimens for individuals with chronic Hepatitis B virus (HBV) infection. Our HBV portfolio includes three novel, wholly owned small molecule inhibitors of the HBV core protein targeting multiple steps of the HBV life cycle, and all three are clinical-stage candidates.

During 2019, we made significant scientific progress with ABI-H0731 (731), our first-generation core inhibitor candidate. Our Phase 2 data set puts us on a path to greater chronic suppression of HBV viral replication (and related consequences of HBV infection), as well as, we believe, toward potential "cures." **With the successful completion of our two Phase 2, 24-week treatment studies (201 and 202), we were encouraged to see that 731 administered with nucleos(t)ide therapy (Nrtl) was well tolerated. 731 also demonstrated both statistically superior antiviral activity in HBV DNA suppression compared to Nrtl alone and significant declines in pgRNA that may indicate decreases in the level of cccDNA, a central component of chronic HBV infection.**

The vast majority of our Phase 2 patients are continuing in our extension study (Study 211) with 731 and Nrtl treatment for up to 76 weeks, at which point we plan to begin transitioning some patients off therapy. For those meeting a set of response criteria suggesting complete suppression of viral replication as measured by our sensitive assays, all HBV treatment will be withdrawn, and we will be able to observe for sustained virologic response (SVR), another key step towards a potential cure. Given this is the first time the SVR concept has been tested in HBV patients receiving regimens containing core inhibitors, we thoughtfully defined the response criteria, developed a clinical monitoring plan, and have sought input from our study investigators and regulators. We expect to provide details on this plan shortly and to begin implementing it during the remainder of the year.

2020

2020 IS AN IMPORTANT YEAR FOR OUR HBV PORTFOLIO:

ABI-H0731—OUR MOST ADVANCED CANDIDATE:

- We expect to begin transitioning patients in Study 211 off treatment based on individual virologic response to observe for SVR.
- We intend to discuss with the regulatory authority in China our plan to initiate studies to enable registration for chronic suppressive therapy, as the health burden of chronic HBV infection there is widespread and significant.
- We continue to explore the potential for collaborative studies combining 731 and Nrtl with other agents that have complementary mechanisms of action, so that we can evaluate triple drug combination regimens in chronic HBV patients.

NEXT-GENERATION CANDIDATES:

- ABI-H2158: We plan to initiate a Phase 2 trial. Data from the first dose cohort of our Phase 1b trial were presented at AASLD 2019, showing potent antiviral activity and tolerability, and final results from the dose-ranging cohorts are among our data sets that have been accepted for presentation at EASL 2020.
- ABI-H3733: We are conducting our first-in-human study, a Phase 1a trial to evaluate safety, tolerability, and pharmacokinetics in healthy volunteers.

PROGRAM UPDATE: Because EASL 2020 has been rescheduled from April to August due to the COVID-19 pandemic, we plan to provide an update on 731 and our HBV core inhibitor portfolio around quarterly reporting in the first half of May.

OUR MICROBIOME PLATFORM: CLINICAL DEVELOPMENT UNDERWAY, PROPRIETARY PROGRAMS ADVANCING

We are developing novel oral live microbial biotherapeutic candidates for a range of important diseases. Our fully integrated proprietary platform includes function-based microbial discovery, in-house scalable GMP manufacturing, and targeted oral delivery technology. Using Assembly's differentiated, scientific approach, individual bacteria and defined consortia are rationally selected for specific biological functions based on our platform of in silico, in vitro, and in vivo capabilities.

We achieved a significant milestone in mid-year 2019, when we dosed our first patient with ABI-M201, our first investigational oral live biotherapeutic product (LBP), as part of our gastrointestinal-focused collaboration with Allergan. Our Phase 1b trial is ongoing, evaluating the safety and efficacy of M201 treatment in patients with mildly to moderately active ulcerative colitis (UC). We look forward to presenting preclinical data on the M201 consortium at the upcoming DDW 2020 Virtual Annual Meeting.

In parallel, we are expanding the potential of our microbiome platform to develop new proprietary LBP candidates for other disease indications. Preclinical data from our immuno-oncology microbiome program have been selected for presentation at the American Association for Cancer Research 2020 Virtual Annual Meeting.

The rescheduled scientific meetings I have mentioned are just one small example of the almost unimaginable impact that the COVID-19 pandemic is having on the lives of people around the world. We have all become acutely aware of how critical health and wellbeing are to our lives. **At Assembly, we recognize that the patients we aim to serve face these concerns every day, and this is why we strive to bring them our potentially transformational treatments as rapidly and effectively as we can.** We are continually reminded of the crucial nature of our efforts, striving to advance health and, especially, to combat other viral diseases.

On an operational level, **our highly experienced team was able to quickly organize and implement plans aimed at mitigating issues arising from the pandemic.** This included early strategies to minimize on-site work and adapt to social distancing directives as the region around our headquarters near San Francisco became one of the first in the country to "shelter in place." The situation is fluid and causes a number of uncertainties beyond our direct control, but we continue to monitor and respond to developments in order to maintain business operations to the extent possible.

I am proud of the focus and scientific approach we bring to our mission and the commitment our employees continue to show as we adapt the way we work in order to achieve our objectives. **Our team has accomplished a great deal since the beginning of 2019, and I believe the Company and its programs are in a strong position. I'm confident that we have the resilience and resources to push toward our goals for 2020 and beyond.**

On behalf of the Assembly team, we are grateful for the support of shareholders like you, and I look forward to updating you on our continued progress in the coming months.

Wishing you good health,

John McHutchison, AO, MD
Chief Executive Officer and President

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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549
FORM 10-K

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

For the fiscal year ended December 31, 2019

or

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

For the Transition Period from _____ to _____

Commission File Number**: 001-35005**

ASSEMBLY BIOSCIENCES, INC.

(Exact name of registrant specified in its charter)

Delaware	**2834**	**20-8729264**
(State or Other Jurisdiction of Incorporation or Organization)	(Primary Standard Industrial Classification Code Number)	(I.R.S. Employer Identification No.)

331 Oyster Point Blvd., Fourth Floor
South San Francisco, California 94080
(Address of Principal Executive Offices)

Registrant's telephone number, including area code: **(833) 509-4583**

Securities Registered Pursuant to Section 12(b) of the Exchange Act:

Title of Each Class	**Trading Symbol(s)**	**Name of Exchange on which Registered**
Common Stock, $0.001 Par Value	ASMB	Nasdaq Global Select Market

Securities Registered Pursuant to Section 12(g) of the Act: None

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

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Exchange 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 (§ 232.45 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

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

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

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

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

The aggregate market value of the voting stock held by non-affiliates of the registrant, as of June 28, 2019, was approximately $332.6 million. Such aggregate market value was computed by reference to the closing price of the common stock as reported on the Nasdaq Global Select Market on June 28, 2019. For purposes of making this calculation only, the registrant has defined affiliates as including only (i) directors, (ii) executive officers, and (iii) certain shareholders that hold greater than 10% of the voting stock of the registrant, in each case, as of June 28, 2019. Shares of common stock held by other persons, including certain other holders of more than 10% of the registrant's outstanding common stock, have not been excluded from the above calculation in that such persons are not deemed to be affiliates. The determination of affiliate status is not necessarily a conclusive determination for other purposes.

As of March 2, 2020, there were 32,624,725 shares of the registrant's common stock, $0.001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

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

ASSEMBLY BIOSCIENCES, INC.
TABLE OF CONTENTS

References to Assembly Biosciences, Inc.

Throughout this Annual Report on Form 10-K, the "Company," "Assembly," "we," "us," and "our," except where the context requires otherwise, refer to Assembly Biosciences, Inc. and its consolidated subsidiaries, and "our board of directors" refers to the board of directors of Assembly Biosciences, Inc.

Forward Looking Information

This Annual Report on Form 10-K contains "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended (the Securities Act) and Section 21E of the Securities Exchange Act of 1934, as amended (the Exchange Act). Such forward-looking statements involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this Annual Report on Form 10-K, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

The forward-looking statements in this Annual Report on Form 10-K include, among other things, statements about:

- the initiation, timing, progress and results of nonclinical studies and clinical studies, and our research and development programs;
- the clinical and therapeutic potential of our product candidates;
- our unproven approaches to therapeutic intervention;
- the potential benefits of our existing collaborations and our ability to establish and maintain collaborations, including with Allergan Pharmaceuticals International Limited;
- our ability to obtain additional funding;
- the timing or likelihood of regulatory filings and approvals for our product candidates;
- the implementation of our business model, strategic plans for our business, product candidates and technology;
- our commercialization, marketing and manufacturing capabilities and strategy;
- the rate and degree of market acceptance for our product candidates, if approved, and their clinical utility;
- our plans to develop and commercialize our product candidates, including in territories outside the United States;
- our ability to retain and recruit key personnel;
- our ability to manage growth;
- our competitive position;
- our intellectual property position;
- our ongoing and planned international operations;
- developments and projections relating to our competitors and our industry; and
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly in the "Risk Factors" section, that could cause actual results or events to differ materially from the forward-looking statements that we make.

You should read this Annual Report on Form 10-K and the documents that we have filed as exhibits to this Annual Report on Form 10-K completely and with the understanding that our actual future results may be materially different from what we expect. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

PART I

Item 1. Business

Overview

We are a clinical-stage biotechnology company advancing two innovative programs: a novel class of oral therapeutic candidates for the treatment of chronic hepatitis B virus (HBV) infection and a novel class of oral live microbial biotherapeutic candidates, which are designed to treat disorders associated with the microbiome.

Over 250 million people worldwide are chronically infected with HBV. Our HBV Cure program is pursuing multiple drug candidates designed to inhibit the HBV lifecycle and block the generation of covalently closed circular DNA (cccDNA), with the aim of increasing the current low cure rate for patients with HBV. We have discovered several novel core inhibitors, which are small molecules that directly target and allosterically modulate the HBV core (HBc) protein.

In recent years, there has been increasing scientific evidence suggesting the therapeutic potential of the human microbiome—the billions of microbes living in and on people-to impact health and disease. Our Microbiome program builds upon experience reported in the literature of successfully treating various disease indications with fecal microbiota transplants (FMT) and seeks to provide a pharmacologically relevant therapy using a "drug like" approach that delivers targeted and specific microbiome therapies in an oral capsule.

Business Strategy

We are focused on enhancing the health and well-being of patients with chronic HBV infection and diseases associated with the microbiome. This commitment drives our efforts to forge a new and differentiated path to treating these conditions, inspired by the needs of millions of affected patients. We are pursuing a portfolio of novel core inhibitors with potential to substantially increase the cure rates of treated HBV patients and a novel class of oral live biotherapeutics designed to provide therapeutic benefit through local and systemic effects. We intend to progress our HBV Cure and Microbiome programs internally or using a variety of strategic arrangements, which may include collaborations, licenses, partnerships and other types of business arrangements. In January 2017, we entered into a Research, Development, Collaboration and License Agreement (the Collaboration Agreement) with Allergan Pharmaceuticals International Limited (Allergan) to develop and commercialize select microbiome gastrointestinal disease therapies. Pursuant to the terms of the Collaboration Agreement, we received from Allergan an upfront payment of $50.0 million in February 2017. Additionally, we are eligible to receive up to approximately $631.0 million in development milestone payments and up to approximately $2.14 billion in commercial development and sales milestone payments contingent upon the successful development and commercialization of licensed compounds for up to six different indications in the gastrointestinal (GI) therapeutic field. We are also eligible to receive tiered royalties at rates ranging from the mid-single digits to the mid-teens based on net sales.

HBV Cure Program

Background

The goal of our HBV Cure program is to substantially increase cure rates for those chronically infected with HBV. HBV is a leading global cause of chronic liver disease and liver transplants. The Centers for Disease Control (CDC) estimates that over 250 million people worldwide are infected with HBV. According to the World Health Organization (WHO), 887,000 people died in 2015 as a result of HBV, mostly from complications, including cirrhosis and hepatocellular carcinoma. HBV is a global epidemic and infects more than twice the number of people infected with hepatitis C virus and HIV infections combined, according to the WHO as of the end of 2018. According to the WHO, as of 2016, of the over 250 million people living with HBV infection, only 27 million were aware of their infection, and only 4.5 million of those diagnosed received treatment. Few treated patients exhibit cure, defined herein as sustained viral suppression (more than six months) of HBV DNA (less than the lower limit of quantification (LLOQ)) after a finite duration of therapy. Despite the low rates of treatment and cure, the current market for nucleos(t)ide reverse transcriptase inhibitors (NrtIs) to treat HBV in the United States, Europe, China, Japan and South Korea was estimated to be approximately $2 billion in 2018. If new therapies can improve cure rates, we believe the market could grow substantially due to an increase in the number of HBV patients expected to seek the new therapies.

Current Treatments

Current therapeutic options for HBV include:

- **Direct Acting Antiviral medications (Nucelos(t)ide analogs).** Several antiviral medications-including lamivudine (Epivir®), adefovir (Hepsera®), telbivudine (Tyzeka®), tenofovir alafenamide (Vemlidy®), tenofovir disoproxil fumarate (Viread®) and entecavir (Baraclude®)-effectively reduce circulating virus levels by inhibiting reverse transcription. Chronic therapy with these agents can result in reduced liver inflammation and fibrosis. Unfortunately, these are rarely curative, even after years of therapy, and viral replication resumes when therapy is stopped.

- **Pegylated Interferon alfa (PegIFN-a).** This synthetic version of a substance produced by the body to fight infection is used mainly for people infected with HBV who do not want to undergo long-term treatment (e.g., patients who might want to become pregnant within a few years). It is administered by injection. Cure rates are relatively low and side effects may be severe, including flu-like symptoms and depression.

Our HBV Cure Program Focus: Targeting HBV Core Protein to Achieve a Cure using Core Inhibitors

Our HBV research team is working on discovering and developing core inhibitors with the potential to inhibit the functional activities of HBV at multiple points in the viral lifecycle. Core protein is involved in several steps of the HBV lifecycle and is essential for HBV's continued regeneration and prolonged survival. In addition to inhibiting viral replication in clinical studies, core inhibitors have been shown to inhibit the generation of closed circular covalent DNA (cccDNA) in preclinical assays.

HBV is a DNA virus that infects hepatocytes and establishes a reservoir of cccDNA, a unique DNA moiety that resides in the cell nucleus of HBV-infected cells and is associated with viral persistence and chronic infection. No current oral therapies target cccDNA activity directly, which makes molecules that can modulate cccDNA generation highly sought in the HBV field. A key focus of our HBV Cure program is targeting the core protein, a highly conserved viral structural protein that has no human homologue and is involved in numerous aspects of the HBV lifecycle, including the generation of the viral cccDNA. We have discovered several chemically distinct series of core inhibitors, which are small molecules that directly target and allosterically inhibit core protein functions. Our HBV pipeline therefore offers the potential for both first in class and best in class opportunities for developing agents that target critical steps involved in cccDNA generation and the viral lifecycle. We believe that our approach of targeting viral core protein and its related functions provides a promising foundation for substantially improving cure rates for HBV infection.

A benchmark for therapeutic agents aiming to decrease cccDNA levels is the use of several key viral antigens as surrogate biomarkers of active cccDNA. The same biomarkers can be used in both primary human hepatocyte cells and patients. On this basis, our core inhibitors have shown preclinical proof of principle. In a variety of cell culture models, core inhibitors have demonstrated the ability to reduce production of viral HBV DNA levels as well as the surrogate markers for cccDNA establishment: HBV e antigen (HBeAg), HBV core related antigen (HBcrAg), HBV surface antigen (HBsAg) and viral pre-genomic RNA (pgRNA). Long-term clinical data from some patients treated with our lead HBV core inhibitor product candidate, ABI-H0731 (731), and NrtI therapy for 16 to 60 weeks has demonstrated a correlation between greater than 3 log reductions in HBV pgRNA levels with multi-log reductions in HBeAg, HBcrAg and HBsAg in patients with HBeAg-positive chronic HBV.

While the goal of our HBV Cure program is to substantially increase cure rates for patients with chronic HBV infection, patients are our first priority. If our product candidates result in improvements to the current standard of care with potential benefit for patients, we would expect to continue to progress them through clinical development and the regulatory approval process for a chronic suppressive indication while continuing to pursue a finite treatment indication with higher cure rates for patients with chronic HBV infection.

Our Product Candidates

Our clinical strategy encompasses testing core inhibitors first as a monotherapy in Phase 1, as required by regulatory agencies, to demonstrate their intrinsic antiviral activity and subsequently in Phase 2 in combination with other classes of HBV therapies.

ABI-H0731

In November 2019, at the American Association for the Study of Liver Diseases Annual Meeting (The Liver Meeting®), we presented final 24-week data from HBeAg-positive patients enrolled in our Phase 2 studies of 731, our lead HBV core inhibitor product candidate—ABI-H0731-201 (Study 201 in NrtI-suppressed patients) and ABI-H0731-202 (Study 202 NrtI-naïve patients). In addition, we presented interim data from an ongoing open-label extension study ABI-H0731-211 (Study 211), where all patients received a combination of 731 and NrtI therapy.

In this analysis, of the 97 patients completing Study 201 or Study 202, 87 were currently receiving a combination of 731 and NrtI therapy and had been treated for at least 16 weeks in Study 211 (cumulative duration of treatment with 731 and NrtI therapy of 16 to more than 40 weeks). 731 was well-tolerated when administered in combination with NrtI therapy with no patients discontinuing treatment due to adverse events (AEs).

As previously reported in the literature, the vast majority of long-term NrtI treated HBeAg-positive patients continue to have low level infectious virus, which was confirmed in Study 201 patients at the time of their enrollment. Final Week 24 results from the HBeAg-positive patients (n=47) demonstrated that, among those with detectable HBV DNA at baseline, 22 out of 27 (81%) of patients treated with 731 and NrtI therapy achieved target not detected (TND) by Week 24 compared to zero out of 12 (0%) patients treated with NrtI therapy only ($p<0.001$), as measured with a highly sensitive PCR assay (LLOQ 5 = IU/mL). These results indicate that the addition of 731 to ongoing NrtI therapy reduced viral burden to levels not achieved by NrtI therapy alone.

Final Week 24 results from treatment-naïve HBeAg-positive patients in Study 202 (n=25) demonstrated faster and deeper HBV DNA declines in patients receiving 731 and entecavir (ETV) than those receiving ETV alone. Statistically significant reductions of pgRNA were observed by Week 2 with 731 and ETV ($p<0.001$).

Longer-term treatment with 731 and NrtI therapy resulted in deeper reductions in HBV DNA and pgRNA. In the analysis, 21 out of 25 patients from Study 202 who were in treatment in Study 211 demonstrated mean HBV DNA and pgRNA declines from baseline of 6.3 logs and 3.0 logs, respectively, at Week 48. Of the 27 NrtI-suppressed HBeAg-positive patients who had received 731 and NrtI therapy for at least 40 weeks in Study 201 and were on treatment in Study 211, 18 (67%) achieved HBV DNA TND + pgRNA less than 35 U/mL, along with significant declines in HBeAg and HBcrAg levels in some of these patients.

An important finding based on interim data from Study 211 is the observed correlation between pgRNA and viral antigens. Eleven out of 21 (52%) patients from Study 202 that are now on Study 211 who have been treated with 731 and NrtI therapy for 16 to 60 weeks have achieved decreases in pgRNA of greater than 3 logs. The results in the table below demonstrate that these larger declines in pgRNA were associated with observed reductions in viral antigens. As cccDNA is the only known source of pgRNA, significant declines in pgRNA, coupled with multi-log declines in viral antigens in some patients, suggests that cccDNA pool levels may be decreasing.

Number	<40 U/L	Log_{10} Decrease	Mean Log Reductions at Last Time Point (range)			Patients Exhibiting ≥0.5 Log Decline (%)		
Patients	ALT	pgRNA	HBeAg	HBcrAg	HBsAg	HBeAg	HBcrAg	HBsAg
11	10	>3.0	1.03 (0.0-2.5)	1.42 (0.0-3.1)	0.86 (0.0-3.6)	9 (82)	10 (91)	6 (55)
8	8	2.0-3.0	0.34 (0.1-0.7)	0.45 (0.1-1.0)	0.14 (0.0-0.5)	2 (25)	6 (75)	1 (13)
2	2	<2.0	0.15 (0.9-1.8)	0.29 (0.3-0.3)	0.17 (0.0-0.3)	0 (0)	0 (0)	0 (0)

From the final summary of safety findings in Study 201 and Study 202, 731 when administered with a NrtI therapy for 24 weeks was well-tolerated in both HBeAg-positive and -negative patients with no AEs leading to discontinuation, no Grade 3 or 4 AEs and no serious AEs reported. Five patients receiving 731 and NrtI reported a rash (four Grade 1 and one Grade 2). No associated systemic signs or laboratory abnormalities were observed, and all patients continued treatment through Week 24. Overall, laboratory abnormalities observed were of Grade 1 or 2 severity and occurred in similar proportions of patients across the two treatment groups. With longer-term ongoing treatment in Study 211, interim data indicated that the nature, frequency and severity of AEs and laboratory abnormalities observed were similar to those observed during the initial 24-week treatment period. Study 211 is ongoing, and we expect to continue to report interim, as well as final, data from this study.

Final data from our completed Phase 1a (ABI-H0731-102) PK, safety and tolerability study and Phase 1b (ABI-H0731-101b) study presented at the Annual Meeting of the European Association for the Study of the Liver (EASL) in April 2018 showed antiviral activity observed across all patient cohorts. In the 300 mg dose cohort, the mean maximal declines from baseline were reported as ≥2.8* log_{10} IU/mL after 28 days, with ≥2.9 and 2.5* log_{10} IU/mL mean declines in HBeAg positive and negative patients, respectively. Maximal viral load declines of 3.6 to 4.0 log_{10} IU/mL were observed in HBeAg negative patients treated at all dose levels (100 mg to 400 mg). Mean pgRNA reductions observed in the 300 mg dose cohort were 2.3 log_{10} IU/mL over 28 days. We believe the observed

reductions in pgRNA levels are a distinguishing feature of this class of inhibitors compared to standard of care NrtI therapy.

Across all cohorts in the Phase 1a and Phase 1b studies, 731 was generally well-tolerated. No serious adverse effects or dose-limiting toxicities were identified, and there was no pattern of treatment emergent clinical or laboratory abnormalities observed. With the exception of an isolated Grade 3 rash at the 400 mg dose that resolved with no intervention required other than treatment discontinuation, there were no other Grade 3 or Grade 4 AEs, and no other drug discontinuations have occurred in these studies.

ABI-H2158

ABI-H2158 (2158), our second product candidate in the HBV Cure program, is internally discovered and developed and is chemically distinct from 731. In preclinical studies, 2158 has demonstrated increased potency compared to 731, particularly related to prevention of cccDNA generation. In November 2018, we initiated a Phase 1a/1b dose-ranging clinical study of 2158 to assess the safety, tolerability and PK of 2158 in healthy volunteers and then subsequently assess the safety, tolerability, PK and initial antiviral potency in non-cirrhotic patients with chronic HBV infection.

We presented final data from the Phase 1a portion of the Phase 1a/1b dose-ranging clinical study at the Annual Meeting of the EASL in April 2019. The Phase 1a study assessed safety, tolerability and PK in 48 healthy volunteers. 2158 was well tolerated following single and multiple ascending doses. There were no dose dependent treatment-emergent AEs and no pattern of clinical safety or laboratory abnormalities observed within or across any cohorts. Once daily administration is projected to result in trough liver concentrations in excess of the in vitro EC50 of 334 nM at which cccDNA establishment is inhibited by 50%.

We initiated the Phase 1b dose-ranging portion of this study in April 2019 to assess the safety, PK and antiviral activity of 2158 in patients with chronic HBV infection.

In November 2019, at The Liver Meeting®, we reported interim data from the first, low-dose cohort of the Phase 1b portion of the Phase 1a/1b dose-ranging clinical study, which is currently enrolling HBeAg-positive patients in sequential dose cohorts of nine patients, with each cohort randomized to receive oral 2158 or placebo (7:2) once daily for 14 days. The interim data from the initial cohort receiving the lowest dose of 2158 at 100 mg demonstrated potent antiviral activity at this initial dose level, reflected by mean declines from baseline to day 15 of 2.3 $\log_{10}$ [range 1.7 – 3.0] and 2.1 $\log_{10}$ [range 1.5 – 2.7] in HBV DNA and pgRNA, respectively.

No serious AEs, dose limiting toxicities or premature discontinuations have been reported to date. All AEs were Grade 1. One patient assigned to placebo and three patients on 2158 reported AEs that resolved without intervention (dizziness, fatigue, rash, headache and upper abdominal pain). Observed steady-state exposures were in excess of the EC90 for in vitro antiviral and cccDNA assays. We believe that the safety and PK data and parameters from this interim analysis support once daily administration and the continued evaluation of 2158 across the planned dose cohorts in patients with chronic HBV infection. Following completion of the Phase 1b dose-ranging study, we expect to initiate a Phase 2 clinical study in the second quarter of 2020.

ABI-H3733

ABI-H3733 (3733), our third product candidate in the HBV Cure program, has completed Investigational New Drug (IND) enabling studies. 3733 has a novel chemical scaffold separate from both 731 and 2158. We presented a preclinical profile of this candidate at EASL in April 2019. In preclinical studies, 3733 demonstrated potent inhibitory activity against multiple steps in the HBV infection cycle, particularly those relating to cccDNA generation. 3733 has shown favorable physical properties and PK profile in multiple species, along with a low drug-drug interaction potential. In preclinical mechanism of action studies, 3733 has shown enhanced potency in blocking encapsidation of pgRNA and disruption of pre-formed capsids as compared to our other product candidates, and in premature disassembly during trafficking of relaxed circular (rc) DNA containing capsids to the nucleus during infection. 3733 inhibited cccDNA formation with an EC50 of 125 nM. 3733's enhanced potency and favorable preclinical results support advancement into Phase 1a studies, which we expect to initiate in the first quarter of 2020.

* Excludes one subject found to have pre-existing core inhibitor resistance substitutions at baseline.

Additional Product Candidates

We plan to conduct additional research and development to identify additional product candidates for our HBV Cure program.

License Agreement and Intellectual Property

Indiana University Research and Technology Corporation

In September 2013, we entered into an exclusive license agreement (the IURTC License Agreement) with Indiana University Research and Technology Corporation (IURTC) pursuant to which we acquired, with rights to sublicense, the rights to develop and commercialize products associated with multiple patents and patent applications covering aspects of our HBV program held by IURTC. As part of this agreement, we are obligated to make milestone payments based upon the successful accomplishment of clinical and regulatory milestones. The aggregate amount of all performance milestone payments under the IURTC License Agreement, should all performance milestones through development be met, is $0.8 million, with a portion related to the first performance milestone having been paid. Under the IURTC License Agreement, we are also obligated to pay IURTC royalties based on net sales of the licensed technology ranging from 0.5% to 1.75%. In addition, under the IURTC License Agreement, we pay annual diligence maintenance fees of $0.1 million. Milestone payments received by IURTC are fully creditable against the annual diligence maintenance fee for the year in which the milestone payments are received.

The IURTC License Agreement may be terminated by us, with or without cause, upon 90 days advance written notice, by IURTC upon our material breach with 60 days advance written notice or by IURTC, in certain cases, upon our insolvency or bankruptcy immediately upon written notice.

Intellectual property

In regard to our HBV patent estate, we co-own with and exclusively license from Indiana University two issued U.S. patents and related foreign patents and patent applications that relate to compositions of matter and methods of using 731. The issued U.S. patents are expected to expire in 2035 and 2036. In addition, we own a pending U.S. patent application and related foreign applications directed to a process for preparing 731; any patents issuing therefrom are expected to expire in 2038. We also own a provisional patent application directed to formulations of 731. Finally, we co-own and exclusively license additional pending U.S. patent applications and related foreign patent applications directed to analogs of 731.

We own a pending U.S. patent application and related foreign applications that relate to compositions of matter and methods of using 2158; any patents issuing therefrom are expected to expire in 2038. We also own two additional PCT patent applications directed to analogs of 2158.

We own an international (PCT) patent application that relates to compositions of matter and methods of using 3733.

Microbiome Program

Background

Our Microbiome program consists of a fully integrated platform that includes a strain isolation, identification, characterization and function based selection process, methods for strain purification and growth under conditions compliant with Good Manufacturing Practice (cGMP) requirements, and a licensed patented delivery system that we call GEMICEL®, which is designed to allow for targeted oral delivery of live biologic and conventional therapies to the lower GI tract.

Our Product Candidates

ABI-M201

We have completed nonclinical studies on our Microbiome program's lead candidate, ABI-M201 (M-201). We filed an IND application in December 2018 for M201, and in February 2019, we initiated a Phase 1b human clinical study of M201 to evaluate the safety of M201 and its effects on disease activity measures in patients with mildly to moderately active ulcerative colitis (UC) and ongoing treatment with mesalamine. The study's primary objective is safety and tolerability, and its secondary objectives focus on the effect of M201 treatment in patients with UC.

The study will consist of two sequential, non-overlapping cohorts of patients, separated by intervening interim analysis. Both cohorts will involve eight weeks of study drug treatment. Interim data from the initial treatment cohort (Cohort A), consisting of 20 patents, will inform the decision to advance to the second cohort (Cohort B), consisting of 24 patients, and its dose selection. The patients in Cohort A will be randomized 1:1 to receive either one daily capsule of M201 or placebo in addition to their treatment with mesalamine. The patients in Cohort B will be randomized 3:1 to receive between one to five daily capsules of M201 or placebo in addition to their treatment with mesalamine. In June 2019, we initiated dosing of the first patient in this clinical study.

Additional Product Candidates

Using our microbiome platform capabilities, we are also exploring additional product candidates for other disease indications, including Crohn's disease (CD) and irritable bowel syndrome (IBS) in connection with the Collaboration Agreement, as well as immune-mediated and metabolic disorders and oncology, which indications we will pursue either internally or in collaboration with other third parties.

Collaboration Agreement

Allergan

On January 6, 2017, we entered into the Collaboration Agreement to develop and commercialize select microbiome gastrointestinal programs. Pursuant to the Collaboration Agreement, we granted Allergan an exclusive worldwide license for rights to preclinical compounds M201 and ABI-M301, targeting UC and CD, respectively, as well as two additional compounds to be identified by us for IBS.

Under the Collaboration Agreement, we and Allergan will collaborate on research and development activities with respect to the licensed compounds in accordance with a mutually agreed upon research and development plan.

Pursuant to the terms of the Collaboration Agreement, we received from Allergan an upfront payment of $50.0 million in February 2017. Additionally, we are eligible to receive up to approximately $631.0 million in development milestone payments and up to approximately $2.14 billion in commercial milestone payments contingent upon the successful development and commercialization of licensed compounds for up to six different indications. We are also eligible to receive tiered royalties at rates ranging from the mid-single digits to the mid-teens based on net sales. We and Allergan have agreed to share development costs up to an aggregate of $75.0 million through proof-of-concept (POC) studies on a ⅓, ⅔ basis, respectively, and Allergan has agreed to assume all post-POC development costs. In the event any pre-POC development costs exceed $75.0 million in the aggregate, we may elect either (a) to fund one-third of such costs in excess of $75.0 million or (b) to allow Allergan to deduct from future development milestone payments one-third of the development costs funded by Allergan in excess of $75.0 million plus a premium of 25%. We have an option to co-promote the licensed programs in the United States and China, subject to certain conditions set forth in the Collaboration Agreement.

Allergan may terminate the Collaboration Agreement at any time upon either 90 days' (prior to the initiation of the first POC trial of a licensed product) or 120 days' (after the initiation of the first POC trial of a licensed product), as applicable, advance written notice to us. The Collaboration Agreement also contains customary provisions for termination by either party, including in the event of breach of the Collaboration Agreement, subject to cure.

License Agreement and Intellectual Property

Therabiome

In November 2013, we entered into a License and Collaboration Agreement with Therabiome, LLC (Therabiome) for all intellectual property and know-how owned or controlled by Therabiome relating to the oral delivery of pharmaceutical drugs to specific sites in the intestine, using a pH-sensitive controlled release capsule-in-capsule technology. Under the agreement, Therabiome granted us the exclusive worldwide license, with rights to sublicense, to develop the intellectual property for commercialization of the use of bacteria, viruses, proteins, and small molecules by oral delivery using the licensed intellectual property in (i) gastrointestinal dysbiosis, including but not limited to irritable bowel syndrome-constipation, irritable bowel syndrome-diarrhea, inflammatory bowel disease, metabolic syndrome, type 2 diabetes, obesity and hypertension, (ii) auto-immune disorders and autism, including but not limited to as controlled by bacteria or virus, and (iii) orally delivered vaccines, including viral and bacterial, and (b) any oral delivery of small molecules using the licensed intellectual property. We are solely responsible for all research and development activities with respect to any product we develop under the license.

For each product or therapy utilizing the licensed technology for which we file a new drug application (NDA), we would be obligated to pay Therabiome aggregate clinical and U.S. regulatory milestone payments ranging from $2.6 million to $3.4 million, depending on whether the milestone occurs before we file our first NDA for a product or after our first, second or third NDA filings. Additional milestone payments of $3.0 million and $1.0 million would be due upon receipt of marketing approval by the FDA and upon approval of a supplemental NDA for a new indication in the United States, respectively.

We also must pay Therabiome lesser amounts for certain foreign regulatory milestones, which vary by country and region. We also must pay Therabiome royalties on annual net product sales in the low to mid-single digit percentages plus, once annual net sales exceed two specified thresholds, a one-time cash payment upon reaching each threshold.

This agreement may be terminated by us, with or without cause, upon 90 days prior written notice, by either party upon the other party's material breach with 180 days prior written notice or by either party upon the other party's challenge of the validity or enforceability or any issued patent within the licensed intellectual property with 90 days prior written notice. Additionally, either party may terminate the agreement upon an event of bankruptcy with respect to the other party.

Intellectual property

In regard to our microbiome patent estate, we exclusively license from Therabiome, two issued U.S. patents, two pending U.S. patent applications, ten patents granted in foreign jurisdictions including Europe, China, Hong Kong, Japan, Australia, and Canada, and related foreign patent applications that relate to a lower gastrointestinal tract-targeted oral delivery system and methods of use thereof. The issued U.S. patents are expected to expire in 2034. The pending U.S. patent applications, if or when issued, are expected to expire between 2033 and 2034. The foreign patents and any patents issuing from the foreign patent applications are expected to expire between 2033 and 2034. In addition, we own one pending U.S. non-provisional patent application and one pending PCT patent application that relates to M201. We also own six provisional patent applications that relate to additional microbiome-related compositions of matter and methods of use thereof.

In addition, we own the GEMICEL® trademark used in conjunction with our licensed targeted oral delivery system.

Government Regulation

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, including any manufacturing changes, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, import and export of pharmaceutical and biological products, such as those we are developing.

U.S. drug approval process

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act (FDCA) and implementing regulations, and biological products under both the FDCA and the Public Health Service Act (PHSA) and implementing 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 U.S. 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, license revocation, imposition of a clinical hold, issuance of warning letters and untitled 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 drug or biological product may be marketed in the United States generally involves the following:

- completion of nonclinical laboratory tests and animal studies in compliance with the FDA's good laboratory practice (GLP) regulations, as required;

- submission to the FDA of an IND which must become effective before human clinical studies may begin;

- approval by an independent institutional review board (IRB) at each clinical site before each trial may be initiated;

- performance of adequate and well-controlled human clinical studies in accordance with good clinical practices (GCP) to establish the safety and efficacy of the proposed drug or biological product for each indication;

- submission to the FDA of a new drug application (NDA) or a biologics license application (BLA);

- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing practices (cGMP) requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity; and

- FDA review and approval of the NDA or BLA.

Nonclinical studies and IND

Nonclinical studies include laboratory evaluation of product chemistry and formulation, as well as *in vitro* and animal studies to assess the potential for adverse events and in some cases to establish a rationale for therapeutic use. The conduct of nonclinical studies is subject to federal regulations and requirements, including GLP regulations for safety/toxicology studies. An IND sponsor must submit the results of the nonclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical studies, among other things, to the FDA as part of an IND. Some long-term nonclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted. For some products, the FDA may waive the need for certain nonclinical tests. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical studies and places the trial on clinical hold. If an IND or clinical study is placed on clinical hold, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical study can begin. As a result, submission of an IND may not result in the FDA allowing clinical studies to commence.

Clinical studies

Clinical studies involve the administration of the investigational new drug or biological product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical study. Clinical studies are conducted under written study protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. A protocol for each clinical study and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, an IRB at each institution participating in the clinical study must review and approve the plan for any clinical study before it commences at that institution, and the IRB must conduct continuing review. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. Information about certain clinical studies must be submitted within specific timeframes to the National Institutes of Health for public dissemination at www.clinicaltrials.gov.

Human clinical studies are typically conducted in three sequential phases, which may overlap or be combined:

- *Phase 1:* The drug or biological product is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness.

- *Phase 2:* The drug or biological product is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.

- *Phase 3:* The drug or biological product is administered to an expanded patient population in adequate and well-controlled clinical studies to generate sufficient data to statistically confirm the efficacy and safety of

the product for approval, to establish the overall risk-benefit profile of the product and to provide adequate information for the labeling of the product.

Progress reports detailing the results of the clinical studies must be submitted at least annually to the FDA. Additionally, IND safety reports must be submitted to the FDA and the investigators within 15 calendar days after determining that the information qualifies for reporting. IND safety reports are required for serious and unexpected suspected adverse reactions, findings from animal or *in vitro* testing or other studies that suggest a significant risk to humans, and any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. In addition, a sponsor must notify the FDA within seven calendar days after receiving information concerning any unexpected fatal or life-threatening suspected adverse reaction. Phase 1, Phase 2 and Phase 3 clinical studies may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical study 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 study at its institution if the clinical study is not being conducted in accordance with the IRB's requirements or if the drug or biological product has been associated with unexpected serious harm to patients.

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

Marketing approval

Assuming successful completion of the required clinical testing, the results of the nonclinical studies and clinical studies, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA or BLA requesting approval to market the product for one or more indications. Under federal law, the submission of most NDAs and BLAs is additionally subject to a substantial application user fee, currently approximately $2.9 million and the sponsor of an approved NDA or BLA is also subject to an annual program fee currently set at approximately $0.3 million through September 30, 2020. These fees are typically adjusted on October 1 each year.

The FDA conducts a preliminary review of all NDAs and BLAs within the first 60 days after submission before accepting them for filing to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA or BLA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to specified performance goals in the review of NDAs and BLAs. Under these goals, the FDA has committed to review most original applications for non-priority products within ten months, and most original applications for priority review products, that is, drugs and biological products for a serious or life-threatening condition that the FDA determines represent a significant improvement over existing therapy, within six months. For NDAs for novel products and all BLAs, the ten- and six-month time periods runs from the filing date; for all other original applications, the ten- and six-month time periods run from the submission date. The review process may be extended by the FDA for three additional months to consider certain information or clarification regarding information already provided in the submission. Despite these review goals, it is not uncommon for FDA review of an NDA or BLA to extend beyond the goal date. The FDA may also refer applications for novel drugs or products that 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. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA or BLA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. In addition, before approving an NDA or BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP and integrity of the clinical data submitted.

After the FDA's evaluation of the NDA or BLA and inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the drug or biological product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA or BLA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval and refuse to approve the NDA or BLA. Even if the FDA approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical studies, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms, including Risk Evaluation and Mitigation Strategies (REMS), which can materially affect the potential market and profitability of the product or impose new labeling, testing or distribution and use requirements. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Fast track designation

The FDA is required to facilitate and expedite the development and review of drugs and biological products that are intended for the treatment of a serious or life-threatening disease or condition for which there is no effective treatment and which demonstrate the potential to address unmet medical needs for the disease or condition. Under the fast track program, the sponsor of a new product candidate may request the FDA to designate the product for a specific indication as a fast track product concurrent with or after the filing of the IND for the product candidate. The FDA must determine if the product candidate qualifies for fast track designation within 60 calendar days after receipt of the sponsor's request.

In addition to other benefits, such as the ability to have greater interactions with the FDA, the FDA may initiate review of sections of a fast track product's NDA or BLA before the application is complete. This rolling review is available if the applicant provides and the FDA approves a schedule for the submission of the remaining information and the applicant pays applicable user fees. However, the FDA's time period goal for reviewing a fast track application does not begin until the last section of the NDA or BLA is submitted. In addition, the fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical study process. In 2018, the FDA granted fast track designation to 731 for the treatment of patients with chronic HBV infection.

Priority review

Under FDA policies, a product candidate may be eligible for priority review, a review generally within a six-month time frame from the time a complete application is received or filed. Products generally are eligible for priority review if they are intended for treatment of a serious or life-threatening disease or condition and provide a significant improvement in safety or effectiveness compared to marketed products in the treatment, diagnosis or prevention of a serious disease or condition. A fast track designated product candidate would ordinarily meet the FDA's criteria for priority review.

Accelerated approval

Under the FDA's accelerated approval regulations, the FDA may approve a drug or biological product for a serious or life-threatening illness that provides meaningful therapeutic benefit to patients over existing treatments based upon a surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality (IMM). In clinical studies, a surrogate endpoint is a measurement of laboratory or clinical signs of a disease or condition that substitutes for a direct measurement of how a patient feels, functions or survives. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. A product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical studies to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the drug from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

Breakthrough therapy designation

A sponsor can request designation of a product candidate as a "breakthrough therapy." A breakthrough therapy is defined as a drug or biological product that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug or biological product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Drugs and biological products designated as breakthrough therapies also may be eligible for priority review. The FDA must take certain actions, such as holding timely meetings and providing advice, intended to expedite the development and review of an application for approval of a breakthrough therapy. Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Orphan drugs

Under the Orphan Drug Act, as amended, the FDA may grant orphan drug designation to drugs or biological products intended to treat a rare disease or condition, which is generally defined as a disease or condition that affects fewer than 200,000 individuals in the United States or that affects more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making available the drug or biologic for the disease or condition will be recovered from sales of the product in the United States. Orphan drug designation must be requested before submitting an NDA or BLA. After the FDA grants orphan drug designation, the identity of the product and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not shorten the duration of the regulatory review and approval process. The first NDA or BLA applicant to receive FDA approval for a particular active moiety to treat a particular disease with FDA orphan drug designation is entitled to a seven-year exclusive marketing period in the United States for that product and indication. During the seven-year exclusivity period, the FDA may not approve any other applications to market the same drug or biological product for the same orphan indication, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity. A drug or biological product will be considered clinically superior if it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug exclusivity does not prevent the FDA from approving a different drug or biological product for the same orphan disease or condition, or the same drug or biological product for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the NDA/BLA application user fee.

Pediatric information

Under the Pediatric Research Equity Act of 2003, as amended, an NDA, BLA or supplement to an NDA or BLA for drug or biological products with certain novel features (e.g., new active ingredient, new indication) must contain data that are adequate to assess the safety and effectiveness of the drug or biological product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. A sponsor of a new drug or biological product subject to the above pediatric testing requirements also is required to submit to the FDA a pediatric study plan generally 60 days after an end-of-Phase 2 meeting with the agency. Generally, the pediatric data requirements do not apply to products with orphan drug designation.

Combination products

The FDA regulates combinations of products that cross FDA centers, such as drug, biologic or medical device components that are physically, chemically or otherwise combined into a single entity, as a combination product. The FDA center with primary jurisdiction for the combination product will take the lead in the premarket review of the product, with the other center consulting or collaborating with the lead center.

The FDA's Office of Combination Products (OCP) determines which center will have primary jurisdiction for the combination product based on the combination product's "primary mode of action." A mode of action is the means by which a product achieves an intended therapeutic effect or action. The primary mode of action is the mode of action that provides the most important therapeutic action of the combination product, or the mode of action expected to make the greatest contribution to the overall intended therapeutic effects of the combination product.

Often it is difficult for the OCP to determine with reasonable certainty the most important therapeutic action of the combination product. In those difficult cases, the OCP will consider consistency with other combination products raising similar types of safety and effectiveness questions, or which center has the most expertise to evaluate the most significant safety and effectiveness questions raised by the combination product.

A sponsor may use a voluntary formal process, known as a Request for Designation, when the product classification is unclear or in dispute, to obtain a binding decision as to which center will regulate the combination product. If the sponsor objects to that decision, it may request that the agency reconsider that decision.

Other regulatory requirements

Any drug or biological product manufactured or distributed by us pursuant to FDA approvals will be subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval.

The FDA may impose a number of post-approval requirements, including REMS, as a condition of approval of an NDA or BLA. For example, the FDA may require post-marketing testing, including Phase 4 clinical studies, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the areas of production and quality control to maintain cGMP compliance.

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

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

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs and biological products generally may be promoted only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off label uses, and a company that is found to have improperly promoted off label uses may be subject to significant liability.

Additional provisions

In addition to FDA restrictions on marketing of pharmaceutical products, several other types of state and federal laws have been applied to restrict certain marketing practices in the pharmaceutical industry in recent years. These laws include anti-kickback statutes and false claims statutes. The federal anti-kickback statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid or other federally financed healthcare programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other. Violations of the anti-kickback statute are punishable by imprisonment, criminal fines, civil monetary penalties and exclusion from participation in federal healthcare programs. In addition, the Affordable Care Act provides that a claim including items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purpose of the federal False Claims Act. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution or other regulatory sanctions, the exemptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exemption or safe harbor.

Federal false claims laws prohibit any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to have a false claim paid. Recently, several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly inflating drug prices they report to pricing services, which in turn were used by the government to set Medicare and Medicaid reimbursement rates, and for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. In addition, certain marketing practices, including off-label promotion, may also violate false claims laws. The majority of states also have statutes or regulations similar to the federal anti-kickback law and false claims laws, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

Physician Drug Samples

As part of the sales and marketing process, pharmaceutical companies frequently provide samples of approved drugs to physicians. The Prescription Drug Marketing Act (PDMA) imposes requirements and limitations upon the provision of drug samples to physicians, as well as prohibits states from licensing distributors of prescription drugs unless the state licensing program meets certain federal guidelines that include minimum standards for storage, handling and record keeping. In addition, the PDMA sets forth civil and criminal penalties for violations.

Foreign Regulation

In order to market any product outside of the United States, we would need to comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy and governing, among other things, clinical studies, marketing authorization, commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we would need to obtain the necessary approvals by the comparable regulatory authorities of foreign countries before we can commence clinical studies or marketing of the product in those countries. The approval process varies from country to country and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may negatively impact the regulatory process in others.

New Legislation and Regulations

From time to time, legislation is drafted, introduced and passed in Congress that could significantly change the statutory provisions governing the testing, approval, manufacturing and marketing of products regulated by the FDA. In addition to new legislation, FDA regulations and policies are often revised or interpreted by the agency in ways that may significantly affect our business and our products. It is impossible to predict whether further legislative changes will be enacted or whether FDA regulations, guidance, policies or interpretations will be changed or what the effect of such changes, if any, may be.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any drug products for which we may obtain regulatory approval. Sales of any of our product candidates, if approved, will depend, in part, on the extent to which the costs of the products will be covered by third-party payors, including government health programs such as Medicare and Medicaid, commercial health insurers and managed care organizations. The process for determining whether a payor will provide coverage for a drug product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the drug product once coverage is approved. Third-party payors may limit coverage to specific drug products on an approved list, or formulary, which might not include all of the approved drugs for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the trials required to obtain FDA or other comparable regulatory approvals. Our product candidates may not be considered medically necessary or cost-effective. A payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Companies may also need to provide discounts to purchasers, private health plans or government healthcare programs. Third-party reimbursement may not be sufficient to enable us to maintain price levels high enough to realize an appropriate return on our investment in product development. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor.

The containment of healthcare costs has become a priority of federal, state and foreign governments, and the prices of drugs have been a focus in this effort. Third-party payors 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 payors 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 health care 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. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Pricing and reimbursement schemes vary widely from country to country. Some countries provide that drug products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies. For example, the European Union provides options for its member states to restrict the range of drug products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a drug product or may instead adopt a system of direct or indirect controls on the profitability of us placing the drug product on the market. Other member states allow companies to fix their own prices for drug products but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, 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 competitive pressure that may reduce 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 of our products.

The marketability of any products for which we may receive regulatory approval for commercial sale is dependent on the availability of adequate coverage and reimbursement from government and third-party payors. In addition, the emphasis on managed care in the United States has increased and we expect will continue to increase the pressure on drug pricing. Coverage policies, third-party reimbursement rates and drug pricing regulation may change at any time. In particular, in the United States, the Affordable Care Act and its amendment, the Health Care and Education Reconciliation Act (the ACA), contains provisions that may reduce the profitability of drug products, including, for example, increased rebates for drugs sold to Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal health care programs.

Among the provisions of the ACA of importance to our potential drug candidates are the following:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologics;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- expansion of healthcare fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, new government investigative powers, and enhanced penalties for noncompliance;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices (which was increased to 70% as of January 1, 2019 under the Bipartisan Budget Act of 2018 (BBA));
- extension of manufacturers' Medicaid rebate liability;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service Act pharmaceutical pricing program;
- requirements to report financial arrangements with physicians and teaching hospitals;
- a requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

Since its enactment, there have been many judicial, Presidential, and Congressional challenges to numerous aspects of the ACA. On January 20, 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On October 13, 2017, President Trump signed an Executive Order terminating the cost-sharing subsidies that reimburse insurers under the ACA. Several state Attorneys General filed suit to stop the administration from terminating the subsidies, but their request for a restraining order was denied by a federal judge in California on October 25, 2017. The loss of the cost share reduction payments is expected to increase premiums on certain policies issued by qualified health plans under the ACA. Further, on June 14, 2018, the U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than $12 billion in ACA risk corridor payments to third-party payors who argued the payments were owed to them. On December 10, 2019, the U.S. Supreme Court heard arguments in *Moda Health Plan, Inc. v. United States*, which will determine whether the government must make risk corridor payments. The U.S. Supreme Court's decision will be released in the coming months, but we cannot predict how the U.S. Supreme Court will rule. The effects of this gap in reimbursement on third-party payors, the viability of the ACA marketplace, providers, and potentially our business, are not yet known.

In December 2018, the Centers for Medicare & Medicaid Services (CMS) published a final rule permitting further collections and payments to and from certain ACA qualified health plans and health insurance issuers under the ACA risk adjustment program in response to the outcome of the federal district court litigation regarding the method CMS uses to determine this risk adjustment. In addition, CMS published a final rule that would give states greater flexibility, starting in 2020, in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces. In addition, CMS has finalized regulations that would give states greater flexibility in setting benchmarks for insurers in the individual and small group marketplaces, which may have the effect of relaxing the essential health benefits required under the ACA for plans sold through such marketplaces.

The Tax Cuts and Jobs Act of 2017 (the Tax Act) includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas, or the Texas District Court Judge, ruled that the individual mandate is a critical and inseverable feature of the Affordable Care Act, and therefore, because it was repealed as part of the Tax Act, the remaining provisions of the ACA are invalid as well. On December 18, 2019, the Fifth Circuit U.S. Court of Appeals held that the individual mandate is unconstitutional and remanded the case to the lower court to reconsider its earlier invalidation of the full ACA. Pending review, the ACA remains in effect, but it is unclear at this time what effect the latest ruling will have on the status of the ACA and the individual mandate. Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA mandated fees, including the so called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device exercise tax on nonexempt medical devices; however, on December 20, 2019, President Trump signed into law the Further Consolidated Appropriations Act (H.R. 1865), which repeals the Cadillac tax, the health insurance provider tax, and the medical device excise tax.

On October 9, 2019, the Department of Health and Human Services (HHS) Office of Inspector General proposed modifications to federal Anti-Kickback Statute safe harbors which, among other things, may affect rebates paid by manufacturers to Medicare Part D plans, the purpose of which is to further reduce the cost of drug products to consumers. Further, the BBA, among other things, amended the ACA, effective January 1, 2019, to reduce the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole." In July 2018, CMS announced that it is suspending further collections and payments to and from certain ACA-qualified health plans and health insurance issuers under the ACA risk adjustment program pending the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, and, due to subsequent legislative amendments, will remain in effect through 2029 unless additional Congressional action is taken. In January 2013, then President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several providers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding.

There has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs and reform government program reimbursement methodologies for drugs. For example, on September 25, 2019, the Senate Finance Committee introduced a bill intended to reduce Medicare and Medicaid prescription drug prices. Named the Prescription Drug Pricing Reduction Action of 2019, the proposed legislation would restructure the Part D benefit, modify payment methodologies for certain drugs, and impose an inflation cap on drug price increases. An even more restrictive bill was introduced in the House of Representatives on September 19, 2019, the Lower Drug Costs Now Act of 2019, which would require HHS to directly negotiate drug prices with manufacturers. The Lower Drugs Costs Now Act of 2019 has passed out of the House and was delivered to the Senate on December 16, 2019. It is unclear whether either of these bills will make it through both chambers and be signed into law, and if either is enacted, what effect it would have on our business.

Anti-Kickback, False Claims, Fraud and Abuse, and Health Information Privacy and Security Laws and Regulations

If we obtain FDA approval for any of our drug candidates and begin commercializing those drugs in the United States, our operations may be subject to various federal and state fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute, the federal False Claims Act, and physician payment sunshine laws and regulations. These laws may impact, among other things, our proposed sales, marketing and education programs. In addition, we may be subject to patient privacy regulation by both the federal government and the states and foreign jurisdictions in which we conduct our business. The laws that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which prohibits, among other things, knowingly and willfully soliciting, receiving, offering or paying any remuneration (including any kickback, bribe, or rebate), directly or indirectly, overtly or covertly, in cash or in kind, to induce, or in return for, either the referral of an individual, or the purchase, lease, order or recommendation of any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare program, such as the Medicare and Medicaid programs. A person or entity can be found guilty of violating the statute without actual knowledge of the statute or specific intent to violate it. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers, and formulary managers on the other;

- federal civil and criminal false claims laws and civil monetary penalty laws, such as the federal False Claims Act, which impose criminal and civil penalties and authorize civil whistleblower or qui tam actions, against individuals or entities for, among other things: knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent; making a false statement or record material to a false or fraudulent claim or obligation to pay or transmit money or property to the federal government; or knowingly concealing or knowingly and improperly avoiding or decreasing an obligation to pay money to the federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act. Manufacturers can be held liable under the False Claims Act even when they do not submit claims directly to government payors if they are deemed to "cause" the submission of false or fraudulent claims;

- HIPAA, which created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations, or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of the payor (e.g., public or private) and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity can be found guilty of violating HIPAA without actual knowledge of the statute or specific intent to violate it;

- HIPAA, as amended by HITECH, and their respective implementing regulations, which impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates that perform services for them that involve the use, or disclosure of, individually identifiable health information, relating to the privacy, security and transmission of individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions;

- the federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;

- the U.S. federal Food, Drug and Cosmetic Act (FDCA), which prohibits, among other things, the adulteration or misbranding of drugs, biologics and medical devices, and the Public Health Service Act (PHSA), which prohibits, among other things, the introduction into interstate commerce of a biological product unless a biologics license is in effect for that product;

- the federal transparency requirements under the ACA, including the provision commonly referred to as the Physician Payments Sunshine Act, which requires manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program to report annually to the U.S. Department of Health and Human Services information related to payments or other transfers of value made to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made to certain non-physician providers such as physician assistants and nurse practitioners; and

- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers.

Additionally, we are subject to state and non-U.S. equivalents of each of the healthcare laws described above, among others, some of which may be broader in scope and may apply regardless of the payor. Many U.S. states have adopted laws similar to the federal Anti-Kickback Statute, some of which apply to the referral of patients for healthcare services reimbursed by any source, not just governmental payors, including private insurers. In addition, some states have passed laws that require pharmaceutical companies to comply with the April 2003 Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers and/or the Pharmaceutical Research and Manufacturers of America's Code on Interactions with Healthcare Professionals. Several states also impose other marketing restrictions or require pharmaceutical companies to make marketing or price disclosures to the state. There are ambiguities as to what is required to comply with these state requirements and if we fail to comply with an applicable state law requirement, we could be subject to penalties.

In addition, regulators globally are also imposing greater monetary fines for privacy violations. The General Data Protection Regulation (GDPR), which went into effect on May 25, 2018, applies to any company established in the European Union (EU) as well as to those outside the EU if they collect and use personal data in connection with the offering goods or services to individuals in the EU or the monitoring of their behavior. The GDPR enhances data protection obligations for processors and controllers of personal data, including, for example, expanded disclosures about how personal information is to be used, limitations on retention of information, mandatory data breach notification requirements and onerous new obligations on services providers. Noncompliance with the GDPR may result in monetary penalties of up to €20 million or 4% of worldwide revenue, whichever is higher. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations. In addition, the GDPR includes restrictions on cross-border data transfers. The GDPR may increase our responsibility and liability in relation to personal data that we process where such processing is subject to the GDPR, and we may be required to put in place additional mechanisms to ensure compliance with the GDPR, including as implemented by individual countries.

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

Competition

The pharmaceutical and biotechnology industry is very competitive, and the development and commercialization of new drugs and biologics is influenced by rapid technological developments and innovation. We face competition from several companies developing and commercializing products that will be competitive with our drug candidates, including large pharmaceutical and smaller biotechnology companies. Additionally, new entrants may potentially enter the market. For our HBV Cure program, potential competitors include Johnson & Johnson, Roche, Gilead Sciences Inc., GlaxoSmithKline plc, Enanta Pharmaceuticals, Inc., HEC Pharma, Arbutus Biopharma Corp. and Aligos Therapeutics, among others. Additionally, we may face competition from currently available treatments for HBV. For our Microbiome program, our competitors include Johnson & Johnson, Takeda Pharmaceutical Company Ltd, Bristol Myers Squibb Co., Seres Therapeutics, Inc., Vedanta Biosciences, Inc., Finch Therapeutics, Inc., Enterome Bioscience S.A. and Second Genome, Inc. Some of the competitive development programs from these companies may be based on scientific approaches that are similar to our approach, and others may be based on entirely different approaches. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization of products similar to ours or that otherwise target indications that we are pursuing.

Manufacturing

We currently rely on third-party manufacturers to supply the quantities of ABI-H0731, ABI-H2158 and ABI-H3733 used in our clinical and nonclinical studies. We currently have no plans to establish any manufacturing facilities for products for our HBV Cure program. In our Microbiome program, we currently utilize internal and third-party manufacturing to supply quantities of drug substance and drug product for use in ongoing and planned nonclinical studies. Third-party manufacturers are used to supply drug substance for early-stage clinical studies in our Microbiome program. We have transitioned third-party manufacturing of drug product to a small-scale internal manufacturing facility for early-stage clinical studies. As we advance these programs through clinical development and potential commercialization, we expect to expand our internal manufacturing capabilities for drug substance and drug product for our Microbiome program.

Employees

As of December 31, 2019, we had 115 employees and contracts with a number of temporary contractors, consultants and contract research organizations.

Corporate History

We were incorporated in Delaware in October 2005 under the name South Island Biosciences, Inc. (which was changed to Ventrus Biosciences, Inc. in April 2007). On July 11, 2014, we acquired Assembly Pharmaceuticals, Inc., a private company, through a merger with our wholly owned subsidiary (the Merger). In connection with the Merger, we changed our name from Ventrus Biosciences, Inc. to Assembly Biosciences, Inc.

Corporate Information

Our principal executive office is at 331 Oyster Point Blvd., Fourth Floor, South San Francisco, California 94080. Our telephone number is (833) 409-4583.

Available Information

Our website address is *www.assemblybio.com*. We routinely post, or have posted, important information for investors on our website in the "Investors" section. We use this website as a means of disclosing material information in compliance with our disclosure obligations under Regulation FD. Accordingly, investors should monitor the "Investors" section of our website, in addition to following our press releases, Securities and Exchange Commission (SEC) filings, presentations and webcasts. We make available free of charge through our website our press releases, Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and all amendments to those reports as soon as reasonably practicable after electronically filed with or furnished to the SEC.

The information contained on our website is not a part of, and should not be construed as being incorporated by reference, into this report.

The reports filed with the SEC by us and by our officers, directors and significant shareholders are available for review on the SEC's website at *www.sec.gov*.

Item 1A. Risk Factors

This report contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those discussed in this report. Factors that could cause or contribute to these differences include, but are not limited to, those discussed below and elsewhere in this report and in any documents incorporated in this report by reference.

You should carefully consider the following risk factors, together with all other information in this report, including our financial statements and notes thereto, and in our other filings with the Securities and Exchange Commission. If any of the following risks, or other risks not presently known to us or that we currently believe to not be significant, develop into actual events, then our business, financial condition, results of operations or prospects could be materially adversely affected. If that happens, the market price of our common stock could decline, and stockholders may lose all or part of their investment.

Risks Related to Our Business

We have no approved products and currently are dependent on the future success of our HBV Cure and Microbiome programs.

To date, we have no approved products on the market and have generated no product revenues. Our prospects are substantially dependent on our ability to develop and commercialize our HBV and microbiome product candidates. Unless and until we receive approval from the FDA or other regulatory authorities for our product candidates, we cannot sell our product candidates and will not have product revenues. We will have to fund all of our operations and capital expenditures from cash on hand, any future securities offerings or debt financings and any fees we may generate from out-licensing, collaborations or other strategic arrangements. If we are unable to develop and commercialize any product candidates from our HBV Cure and Microbiome programs, we will be unable to generate revenues from the sale of products or build a sustainable or profitable business.

In addition, all of our product candidates are currently in early clinical development or in varying stages of nonclinical development and their risk of failure is high. The data supporting our drug discovery and nonclinical and clinical development programs are derived from either laboratory, nonclinical studies, Phase 1a/1b and ongoing Phase 2a clinical data. We cannot predict when or if any one of our product candidates will prove safe and effective in humans or will receive regulatory approval. The scientific evidence to support the feasibility of our product candidates and therapeutic approaches is limited, and many companies, some with more resources than we have, are and may be developing competitive product candidates. For these and other reasons, our drug discovery and development may not be successful, and we may not generate viable products or revenue.

We depend entirely on the success of product candidates from our HBV Cure program and our Microbiome program. We cannot be certain that we or our collaborators will be able to obtain regulatory approval for, or successfully commercialize, product candidates from either of our current programs or any other product candidates we may subsequently identify.

We and our collaborators are not permitted to market or promote any product candidates in the United States, Europe, China or other countries before we receive regulatory approval from the FDA or comparable foreign regulatory authorities, and we may never receive such regulatory approval for our current product candidates. We have not submitted a BLA or NDA to the FDA or comparable applications to other regulatory authorities and do not expect to be in a position to do so in the foreseeable future.

All of our product candidates are currently in early clinical development or in varying stages of nonclinical development. It may be years before the larger, pivotal trials necessary to support regulatory approval of our product candidates are initiated, if ever. The clinical studies of our product candidates are, and the manufacturing and marketing of our product candidates will be, subject to extensive and rigorous review and regulation by numerous government authorities in the United States and in other countries where we intend to test and, if approved, market any product candidate. Before obtaining regulatory approvals for the commercial sale of any product candidate, we must successfully meet a number of critical developmental milestones, including:

- developing dosages that will be tolerated, safe and effective;
- reaching agreement with the FDA or comparable foreign regulatory authorities regarding the scope, design and data necessary to support regulatory approval for the product candidate;

- demonstrating through clinical studies that the product candidate is safe and effective in patients for the intended indication;

- determining the appropriate delivery mechanism;

- demonstrating that the product candidate formulation will be stable for commercially reasonable time periods; and

- completing the development and scale-up to permit manufacture of our product candidates in quantities sufficient to execute on our clinical development plans and, eventually, in commercial quantities with sufficient quality and at acceptable prices.

The time necessary to achieve these developmental milestones for any individual product candidate is long and uncertain, and we may not successfully complete these milestones for our HBV and microbiome therapies or any other product candidates that we may develop. We have not yet completed and may never complete the development of any products. If we are unable to complete clinical development of our HBV or microbiome therapies, or any other product candidates that we may identify, we will be unable to generate revenue from the sale of products or build a sustainable or profitable business.

Nonclinical studies may not be representative of disease behavior in clinical studies. The outcomes of nonclinical testing and clinical studies are uncertain, and results of nonclinical studies and earlier clinical studies may not be predictive of future clinical study results.

The results of nonclinical studies may not be representative of disease behavior in a clinical setting and thus may not be predictive of the outcomes of our clinical studies. In addition, the results of nonclinical studies and early clinical studies of product candidates may not be predictive of the results of later-stage clinical studies, and the results of any study or trial for any of our product candidates may not be as favorable as the results for any prior studies or trials, if at all.

Nonclinical studies and clinical testing are expensive, can take many years to complete and their outcomes are highly uncertain. Failure can occur at any time during the nonclinical study and clinical study processes due to inadequate performance of a drug candidate or inadequate adherence by patients or investigators to clinical study protocols. Further, clinical studies might not provide statistically significant data supporting a product candidate's safety and effectiveness to obtain the requisite regulatory approvals. In addition, there is a high failure rate for drugs and biologics proceeding through clinical studies. Our failure to replicate earlier positive results in later-stage clinical studies or otherwise demonstrate the required characteristics to support marketing approval for any of our product candidates would substantially harm our business, prospects, financial condition and results of operations.

Top-line or initial data may not accurately reflect the complete results of a particular study or trial.

We may publicly disclose top-line or initial data from time to time, which is based on a preliminary analysis of then-available efficacy, tolerability, PK and safety data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimates, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to evaluate fully and carefully all data. As a result, the top-line or initial 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. Top-line data also remain subject to audit and verification procedures that may result in the final data being materially different from the initial or preliminary data we previously published. As a result, top-line and initial data should be viewed with caution until the final data are available.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of the particular drug candidate or biotherapeutic and our company in general. In addition, the information we may publicly disclose regarding a particular nonclinical or clinical study is based on what is typically extensive information, and you or others may not agree with what we determine is the material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular drug, drug candidate or our business. If the top-line or initial data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed or delayed, which could harm our business, financial condition, operating results or prospects.

Nonclinical and clinical testing required for our product candidates is expensive and time-consuming and may result in delays or may fail to demonstrate safety and efficacy for desired indications. Such delays or failures could delay or prevent our receipt of licensing, sales and/or milestone revenue.

Before we or any commercial partners can obtain FDA approval (or other foreign approvals) necessary to sell any of our product candidates, we must show through nonclinical studies and human testing in clinical studies that each potential product is safe and effective in humans. To meet these requirements, we must conduct extensive nonclinical testing and sufficient adequate and well-controlled clinical studies. Conducting clinical studies is a lengthy, time consuming, and expensive process. The length of time might vary substantially according to the type, complexity, novelty, and intended use of the product candidate, and often can be several years or more per trial. Delays associated with product candidates for which we are directly conducting nonclinical studies or clinical studies might cause us to incur additional operating expenses. The commencement and rate of completion of clinical studies might be delayed by many factors, including, for example:

- delays in reaching agreement with regulatory authorities on trial design;
- delays in reaching agreement on acceptable terms with prospective contract research organizations (CROs) and clinical study sites;
- failure to demonstrate efficacy during clinical studies;
- the emergence of unforeseen safety issues;
- inability to manufacture sufficient quantities of qualified materials under cGMP for use in clinical studies;
- slower than expected rates of patient recruitment;
- failure to recruit a sufficient number of eligible patients, which may be due to a number of reasons, including the size of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the study, the design of the clinical study, and other potential drug candidates being studied;
- delays in having patients complete participation in a trial or return for post-treatment follow-up;
- delays caused by patients dropping out of a trial due to product side effects, disease progression or other reasons;
- clinical sites dropping out of a trial to the detriment of enrollment;
- modification of clinical study protocols;
- delays by our contract manufacturers to produce and deliver sufficient supply of clinical study materials;
- occurrence of adverse events associated with the product candidate that are viewed to outweigh its potential benefits;
- changes in regulatory requirements for clinical studies;
- delays, suspension, or termination of clinical studies by the institutional review board or ethics committee responsible for overseeing the study at a particular study site; and
- government or other regulatory agency delays or clinical holds requiring suspension or termination of our clinical studies.

We have used and intend to continue to rely on one or more CROs to conduct our nonclinical studies and clinical studies. We are highly dependent on these CROs to conduct our studies and trials in accordance with the requirements of the FDA, applicable local laws and good clinical and scientific practice. In the event the CROs fail to perform their duties in such a fashion, we may not be able to complete our clinical studies and may fail to obtain regulatory approval for any of our product candidates.

The failure of nonclinical studies and clinical studies to demonstrate safety and effectiveness of a product candidate for the desired indications could harm the development of that product candidate or other product candidates. This failure could cause us to abandon a product candidate and could delay development of other product candidates. Any delay in, or termination of, our nonclinical studies or clinical studies would delay the filing of our NDAs or BLAs with the FDA and, ultimately, our ability to commercialize our product candidates and generate product revenues. Any change in, or termination of, our clinical studies could materially harm our business, financial condition, and results of operations.

Any product candidates that we may discover and develop may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.

In our industry, many product candidates that initially showed promise in early stage testing have later been found to cause side effects that prevented their further development. Undesirable side effects caused by any product candidates that we may discover or develop, or safety, tolerability or toxicity issues that may occur in our nonclinical studies, clinical studies or in the future, could cause us or regulatory authorities to interrupt, restrict, delay, or halt clinical studies. Such results could also cause us to, or regulatory authorities to require us to, cease further development of our product candidates for any or all targeted indications. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign authorities. Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, prospects, financial condition and results of operations.

Additionally, if any of our product candidates receives marketing approval and we or others later identify undesirable or unacceptable side effects caused by these product candidates, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approvals of such product and require us to take them off the market;
- regulatory authorities may require the addition of labeling statements, specific warnings, a contraindication or field alerts to physicians and pharmacies;
- regulatory authorities may require a medication guide outlining the risks of such side effects for distribution to patients, or that we implement a Risk Evaluation Mitigation Strategy (REMS) plan to ensure that the benefits of the product outweigh its risks;
- we may be required to change the way a product is administered, conduct additional clinical studies or change the labeling of a product;
- we may be subject to limitations on how we may promote the product;
- sales of the product may decrease significantly;
- we may be subject to litigation or product liability claims; and
- our reputation may suffer.

Any of these events could prevent us or any collaborators from achieving or maintaining market acceptance of our product candidates or could substantially increase commercialization costs and expenses, which in turn could delay or prevent us from generating significant revenue from the sale of our product candidates.

We have a limited operating history and a history of operating losses and expect to incur significant additional operating losses.

We merged with Assembly Pharmaceuticals, Inc. (Assembly Pharmaceuticals), a private company, in July 2014. We have only a limited operating history since the merger. Therefore, there is limited historical financial information upon which to base an evaluation of our performance. Our prospects must be considered in light of the uncertainties, risks, expenses, and difficulties frequently encountered by companies in their early stages of operations. We, and Assembly Pharmaceuticals prior to our merger, have generated losses since we began operations and as of December 31, 2019 and December 31, 2018, the combined company had an accumulated deficit of approximately $439.4 million and $341.8 million, respectively, and net losses of approximately $97.6 million, $90.8 million, and $42.8 million for the years ended December 31, 2019, 2018 and 2017, respectively. These net losses have had, and will continue to have, an adverse effect on our stockholders' equity and working capital. We expect to incur substantial additional losses over the next several years as we continue to pursue our research, development, nonclinical studies and clinical study activities. Further, since our initial public offering, we have incurred and will continue to incur as a public company significant additional legal, accounting and other expenses to which we were not subject to as a private company, including expenses related to our efforts in complying with the requirements of the Sarbanes-Oxley Act of 2002 (the Sarbanes-Oxley Act), the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010 and other public company disclosure and corporate governance requirements and responding to requests of government regulators. The amount of future losses and when, if ever, we will achieve profitability are uncertain and will depend, in part, on the rate of increase in our expenses, our ability to generate revenues from the sale of products and our ability to raise additional capital. We have no products that have generated any commercial revenue, do not expect to generate revenues from the commercial sale of products unless and until our HBV or microbiome therapies or any other product candidate is approved by the FDA for sale, and we might never generate revenues from the sale of products.

We are not currently profitable and might never become profitable.

We have a history of losses and expect to incur significant operating and capital expenditures and resultant substantial losses and negative operating cash flow for the next several years and beyond if we do not successfully launch and commercialize any product candidates from our HBV Cure or Microbiome programs. We might never achieve or maintain profitability. We anticipate that our expenses will continue to be substantial in the foreseeable future as we:

- advance 731 and 2158, our first and second HBV product candidates, respectively, through clinical development and conduct nonclinical studies and clinical studies of 3733, our third HBV product candidate;
- advance M201 (UC), our first candidate from our Microbiome program, through Phase 1b clinical development;
- continue to undertake research and development to identify potential additional product candidates in both our HBV Cure and Microbiome programs;
- seek regulatory approvals for our product candidates; and
- pursue our intellectual property strategy.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability. In addition, our expenses could increase if we are required by the FDA or comparable foreign regulatory authorities to perform studies or trials in addition to those currently expected, or if there are any delays in completing our clinical studies or the development of any of our product candidates.

As a result, we will need to generate significant revenues in order to achieve and maintain profitability. Our ability to generate revenue from the sale of products and achieve profitability will depend on, among other things:

- successful completion of research, nonclinical studies and clinical studies for our product candidates;
- obtaining necessary regulatory approvals from the FDA and comparable foreign regulatory authorities for our product candidates;

- maintaining patent protection for our products, methods, processes and technologies and/or obtaining regulatory exclusivity;

- establishing manufacturing, sales, and marketing arrangements internally and/or with third parties for any approved products; and

- raising sufficient funds to finance our activities, if and when needed.

We might not succeed at any of these undertakings. If we are unsuccessful at some or all of these undertakings, our business, prospects, and results of operations might be materially adversely affected.

We are an early stage company and might not be able to commercialize any product candidates.

We are an early stage company and have not demonstrated our ability to perform the functions necessary for the successful commercialization of any product candidates. The successful commercialization of any product candidates will require us to perform a variety of functions, including:

- continuing to undertake research and development and nonclinical studies and clinical studies;

- participating in regulatory approval processes;

- formulating and manufacturing products; and

- conducting sales, marketing and distribution activities.

We currently do not have the infrastructure to manufacture, market and sell our product candidates. If we partner with one or more third-party entities, those commercial partners may demand and receive rights to control product development and commercialization. As a result, these commercial partners may conduct these programs and activities more slowly or in a different manner than expected. If any of these events were to occur, the development of any product candidate could be significantly delayed, more expensive or less lucrative to us than anticipated, any of which would have a significant adverse effect on our business.

Our failure to commercialize successfully our product candidates would negatively impact the value of our company and could impair our ability to raise capital, expand our business, diversify our research and development pipeline, market our product candidates, if approved, or continue our operations.

There are substantial risks inherent in attempting to commercialize new drugs and biologics, and, as a result, we may not be able to develop successfully products for commercial use.

Scientific research and development require significant amounts of capital and takes a long time to reach commercial viability, if it can be achieved at all. To date, our research and development projects have not produced commercially viable drugs or biologics and may never do so. During the research and development process, we may experience technological barriers that we may be unable to overcome. Further, certain underlying premises in our development programs are not fully proven.

Our HBV therapy research and development efforts involve therapeutics based on modulating forms of HBV core proteins with core inhibitors. The development of our core inhibitor technology is in early stages, and the commercial feasibility and acceptance of our core inhibitor technology is unknown. More specifically, while there may be initial indications of decreasing cccDNA levels in some treated patients, the theory that treatment with core inhibitors may result in more rapid loss of cccDNA compared to conventional (standard of care) therapies is unproven. It is also unknown if the biomarkers assumed to be indicators of cccDNA pool levels (such as serum pgRNA, HBeAG, HBcrAg and, to a lesser extent, HBsAg in HBV patients) will be meaningfully altered in patients on treatment with core inhibitors. Additionally, even if core inhibitor technology is successful at targeting the HBV core protein and treatment is successful at reducing cccDNA levels in HBV patients, it may not result in a commercially viable drug if there is not a corresponding medical benefit related to the underlying HBV infection.

Similarly, our Microbiome program is based on a novel therapeutic approach designed to treat disorders associated with the microbiome. To our knowledge, no companies have received regulatory approval for, or manufactured on a commercial scale, any microbiome-based therapeutics. Our microbiome therapy candidates are in nonclinical and early clinical development, and our GEMICEL® dual-targeted release capsule formulation is novel and has not yet shown to deliver successfully live bacteria in patients. The ability to deliver bacteria effectively and reliably to the GI tract is unproven, and, even if it can be proven, it may be difficult or impossible to provide the treatment economically. Because of these uncertainties, it is possible that no commercial products will be successfully developed. If we are unable to develop successfully commercial products, we will be unable to generate revenue from the sale of products or build a sustainable or profitable business.

A Fast Track designation by the FDA may not actually lead to a faster development or regulatory review or approval process.

If a drug or biologic is intended for the treatment of a serious or life-threatening condition and nonclinical or clinical data demonstrate the potential to address unmet medical needs for this condition, the drug or biologic sponsor may apply for FDA Fast Track designation. Fast Track designation provides increased opportunities for sponsor meetings with the FDA during preclinical and clinical development, in addition to the potential for rolling review once a marketing application is filed. The FDA has broad discretion whether or not to grant this designation, and even if we believe a particular product candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. In 2018, the FDA granted Fast Track designation to 731 for the treatment of patients with chronic HBV infection. We may seek Fast Track designation for other product candidates, but there is no assurance that it will be granted. Even with Fast Track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. Fast Track designation does not assure ultimate approval by the FDA. The FDA may withdraw Fast Track designation if it believes that the designation is no longer supported by data from our product development program.

A breakthrough therapy designation by the FDA for our product candidates may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that our product candidates will receive marketing approval.

We may seek a breakthrough therapy designation for our product candidates. A breakthrough therapy is defined as a drug or biologic that is intended to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug or biologic may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. For drugs that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor can help to identify the most efficient path for clinical development. Drugs designated as breakthrough therapies by the FDA may also be eligible for accelerated approval.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a breakthrough therapy designation for a product candidate may not result in a faster development process, review or approval compared to conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our product candidates qualify as breakthrough therapies, the FDA may later decide that the products no longer meet the conditions for qualification and rescind the designation.

We will need additional financing to complete the development of any product candidate and fund our activities in the future.

We anticipate that we will incur operating losses for the next several years as we continue to develop our HBV product candidates and our microbiome platform as well as initiate development of any other product candidates and will require substantial funds during that time to support our operations. We expect that our current resources will provide us with sufficient capital to fund our operations for at least the next twelve months. However, we might consume our available capital before that time if, for example, we are not efficient in managing our resources or if we encounter unforeseen costs, delays or other issues or if regulatory requirements change or if clinical study timelines are accelerated. If that happens, we may need additional financing to continue the development of our HBV and microbiome product candidates, which we might seek and receive from the public financial markets, third-party commercial partners, private placements, debt financings or other sources. There is no assurance that we will

be able to generate sufficient revenue from our Collaboration Agreement with Allergan or that we will be successful in raising any necessary additional capital on terms that are acceptable to us, or at all. If such events or other unforeseen circumstances occurred and we were unable to generate sufficient revenue or raise capital, we could be forced to delay, scale back or discontinue product development, sacrifice attractive business opportunities, cease operations entirely and sell or otherwise transfer all or substantially all of our remaining assets.

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

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

In addition, over the last several years, including most recently from December 22, 2018 to January 25, 2019, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If another prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions or our ability to raise capital through the public financial markets, either of which could have a material adverse effect on our business.

Our Microbiome program is substantially dependent on our Collaboration Agreement with Allergan, which may be terminated or may not be successful due to a number of factors, which could have a material adverse effect on our business and operating results.

In January 2017, we entered into the Collaboration Agreement for the development and commercialization of select microbiome gastrointestinal programs in ulcerative colitis, Crohn's disease and irritable bowel syndrome. Our collaboration with Allergan may be terminated, or may not be successful, due to a number of factors. In particular, Allergan may terminate the Collaboration Agreement at any time upon either 90 days' (prior to the initiation of the first POC trial of a licensed product) or 120 days' (after the initiation of the first POC trial of a licensed product), as applicable, advance written notice to us. The Collaboration Agreement also contains customary provisions for termination by either party, including in the event of breach of the Collaboration Agreement, subject to cure. In addition, if we are unable to identify product candidates for the licensed indications or we are unable to protect our products by obtaining and defending patents, the collaboration could fail. If the collaboration is unsuccessful for these or other reasons, or is otherwise terminated for any reason, we may not receive all or any of the research program funding, milestone payments or royalties under the agreement. Any of the foregoing could result in a material adverse effect on our business, results of operations and prospects and may cause our stock price to decline. In June 2019, Allergan and AbbVie Inc. (AbbVie) announced that they had entered into a definitive transaction agreement under which AbbVie will acquire Allergan. Assuming the conditions to close are satisfied, the acquisition is expected to close in early 2020. We do not know what, if any, impact this transaction will have on the Collaboration Agreement.

We are dependent on a license relationship for each of our HBV Cure program and our Microbiome program.

Our license agreement with IURTC from whom we have licensed 731 and certain other HBV therapies, requires us to make milestone payments based upon the successful accomplishment of clinical and regulatory milestones related to 731 and certain other HBV therapies. The aggregate amount of all performance milestone payments under the IURTC License Agreement, should all performance milestones through development be met, is $825,000, with a portion related to the first performance milestone having been paid. We also are obligated to pay IURTC royalty payments based on net sales of the licensed technology. We are also obligated to pay diligence maintenance fees ($75,000 to $100,000) each year to the extent that the royalty, sublicensing, and milestone payments to IURTC are less than the diligence maintenance fee for that year. Our license with Therabiome, from whom we have licensed a delivery platform for our Microbiome program, also requires us to pay regulatory and clinical milestones as well as

royalty payments to Therabiome. If we breach any of these obligations, we could lose our rights to the targeted delivery mechanism of our Microbiome program. If we fail to comply with similar obligations to any other licensor, then that licensor would have the right to terminate the license, in which event we would not be able to commercialize drug candidates or technologies that were covered by the license. In addition, the milestone and other payments associated with licenses will make it less profitable for us to develop our drug candidates than if we owned the technology ourselves.

Corporate and academic collaborators might take actions to delay, prevent, or undermine the success of our product candidates.

Our operating and financial strategy for the development, nonclinical and clinical testing, manufacture, and commercialization of drug candidates heavily depends on collaborating with corporations, academic institutions, licensors, licensees, and other parties. However, there can be no assurance that we will successfully establish or maintain these collaborations. In addition, should a collaboration be terminated, replacement collaborators might not be available on attractive terms, or at all. The activities of any collaborator will not be within our control and might not be within our power to influence. There can be no assurance that any collaborator will perform its obligations to our satisfaction or at all, that we will derive any revenue or profits from these collaborations, or that any collaborator will not compete with us. If any collaboration is not successful, we might require substantially greater capital to undertake development and marketing of our proposed products and might not be able to develop and market these products effectively, if at all. In addition, a lack of development and marketing collaborations might lead to significant delays in introducing proposed products into certain markets and/or reduced sales of proposed products in such markets.

We rely on data provided by our collaborators and others that has not been independently verified and could prove to be false, misleading, or incomplete.

We rely on third-party vendors, scientists, investigators and collaborators to provide us with significant data and other information related to our projects, nonclinical studies and clinical studies, and our business. If these third parties provide inaccurate, misleading, or incomplete data, our business, prospects, and results of operations could be materially adversely affected.

Research, development and commercialization goals may not be achieved in the timeframes that we publicly estimate, which could have an adverse impact on our business and could cause our stock price to decline.

We set goals, and make public statements regarding our expectations, regarding the timing of certain accomplishments, developments and milestones under our research and development programs. The actual timing of these events can vary significantly due to a number of factors, including, without limitation, the amount of time, effort and resources committed to our programs by us and any collaborators and the uncertainties inherent in the clinical development and regulatory approval process. As a result, there can be no assurance that we or any collaborators will initiate or complete clinical development activities, make regulatory submissions or receive regulatory approvals as planned or that we or any collaborators will be able to adhere to our current schedule for the achievement of key milestones under any of our programs. If we or any collaborators fail to achieve one or more of the milestones as planned, our business could be materially adversely affected, and the price of our common stock could decline.

We lack suitable facilities for certain nonclinical and clinical testing and expect to rely on third parties to conduct some of our research and nonclinical testing and our clinical studies, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such research, testing or trials.

We do not have sufficient facilities to conduct all of our anticipated nonclinical and clinical testing. As a result, we expect to contract with third parties to conduct a significant portion of our nonclinical and clinical testing required for regulatory approval for our product candidates. We will be reliant on the services of third parties to conduct studies on our behalf. If we are unable to retain or continue with third parties for these purposes on acceptable terms, we may be unable to develop successfully our product candidates. In addition, any failures by third parties to perform adequately their responsibilities may delay the submission of our product candidates for regulatory approval, which would impair our financial condition and business prospects.

Our reliance on these third parties for research and development activities also reduces our control over these activities but will not relieve us of our responsibilities. For example, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards, including, in the case of clinical studies, good clinical practices, and our reliance on third parties does not relieve us of our regulatory responsibilities. Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. In addition, these third parties are not our employees, and except for remedies available to us under our agreements with such third parties, we cannot control whether or not they devote sufficient time and resources to our clinical and nonclinical programs. If these third parties 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 research, nonclinical studies or clinical studies may be extended, delayed or terminated and we may not be able to obtain, or may be delayed in obtaining, regulatory approvals for our product candidates. As a result, our results of operations and business prospects would be harmed, our costs could increase and our ability to generate revenues from the sale of products could be delayed.

We will need to either establish our own clinical and commercial manufacturing capabilities or rely on third parties to formulate and manufacture our product candidates. We rely on third parties to manufacture products that we study in combination with our product candidates. Our use of third parties to manufacture these materials may increase the risk that we will not have sufficient quantities of our product candidates or other products, or necessary quantities of such materials on time or at an acceptable cost.

We currently rely on third-party manufacturers to supply the quantities of 731, 2158 and 3733 used in our clinical and nonclinical studies and the drug substance for our Microbiome program. We currently manufacture our microbiome drug product for use in our planned nonclinical studies and early-stage clinical studies; however, we may require third-party manufacturers for subsequent clinical studies or other microbiome drug products. In addition, if any product candidate we might develop or acquire in the future receives FDA or other regulatory approval, we will need to either manufacture commercial quantities of the product on our own or rely on one or more third-party contractors to manufacture our products. The establishment of internal manufacturing capabilities is difficult and costly, and we may not be successful in doing so. If, for any reason, we are unable to establish our own manufacturing capabilities and we are unable to rely on any third-party sources we have identified to manufacture our product candidates, either for clinical studies or, at some future date, for commercial quantities, then we would need to identify and contract with additional or replacement third-party manufacturers to manufacture compounds, drug substance and drug products for nonclinical, clinical and commercial purposes. We might not be successful in identifying additional or replacement third-party manufacturers, or in negotiating acceptable terms with any that we do identify. If we are unable to establish and maintain manufacturing capacity either on our own or through third parties, the development and sales of our products and our financial performance will be materially and adversely affected.

In addition, before we or any of our collaborators can begin to commercially manufacture our product candidates, each manufacturing facility and process is subject to regulatory review. Manufacturing of drugs for clinical and commercial purposes must comply with the FDA's cGMPs and applicable non-U.S. regulatory requirements. The cGMP requirements govern compliance and documentation policies and procedures. Complying with cGMP and non-U.S. regulatory requirements will require that we expend time, money, and effort in production, recordkeeping, and compliance to assure that the product meets applicable specifications and other requirements. Any manufacturing facility must also pass a pre-approval inspection prior to FDA approval. Failure to pass a pre-approval inspection might significantly delay FDA approval of our product candidates. If we or any of our future collaborators fails to comply with these requirements with respect to the manufacture of any of our product candidates, regulatory action could limit the jurisdictions in which we are permitted to sell our products, if approved. As a result, our business, financial condition, and results of operations might be materially harmed.

We are exposed to the following risks with respect to the manufacture of our product candidates:

- If we are unable to establish our own manufacturing capabilities, we will need to identify manufacturers for commercial supply on acceptable terms, which we may not be able to do because the number of potential manufacturers is limited, and the FDA must evaluate any new or replacement contractor. This evaluation would generally require compliance inspections. In addition, a new manufacturer would have to be educated in, or develop substantially equivalent processes for, production of our products after receipt of FDA approval, if any.

- We or any third-party manufacturers with whom we contract might be unable to formulate and manufacture our product candidates in the volume and of the quality required to meet our clinical and, if approved, commercial needs in a timely manner.

- Any third-party manufacturers with whom we contract might not perform as agreed or might not remain in the contract manufacturing business for the time required to supply our clinical studies or to produce, store and successfully distribute our products.

- One or more of any third-party manufacturers with whom we contract could be foreign, which increases the risk of shipping delays and adds the risk of import restrictions.

- Drug manufacturers are subject to ongoing periodic unannounced inspection by the FDA and corresponding state agencies to ensure strict compliance with cGMP and other government regulations and corresponding foreign requirements. Any internal manufacturing facilities we establish may fail to comply, and we would not have complete control over any third-party manufacturers' compliance, with these regulations and requirements.

- We may be required to obtain additional intellectual property rights from third parties in order to manufacture our product candidates, and if any third-party manufacturer makes improvements in the manufacturing process for our product candidates, we might not own, or might have to share, the intellectual property rights to the innovation with our licensors.

- We may be required to share our trade secrets and know-how with third parties, thereby risking the misappropriation or disclosure of our intellectual property by or to third parties.

- If we contract with third-party manufacturers, we might compete with other companies for access to these manufacturers' facilities and might be subject to manufacturing delays if the manufacturers give other clients higher priority than us.

Each of these risks could delay our development efforts, nonclinical studies and clinical studies or the approval, if any, of our product candidates by the FDA or applicable non-U.S. regulatory authorities or the commercialization of our product candidates and could result in higher costs or deprive us of potential product revenues. As a result, our business, financial condition, and results of operations might be materially harmed.

If we or our collaborators cannot compete successfully for market share against other companies, we might not achieve sufficient product revenues and our business will suffer.

If our product candidates receive approval from the FDA or applicable non-U.S. regulatory authorities, they will compete with a number of existing and future drugs and biologics developed, manufactured and marketed by others. Existing or future competing drugs might provide greater therapeutic convenience or clinical or other benefits for a specific indication than our product candidates or might offer comparable performance at a lower cost. If our product candidates fail to capture and maintain market share, we might not achieve sufficient product revenues and our business will suffer.

We might compete against fully integrated pharmaceutical or biotechnology companies and smaller companies that are collaborating with larger pharmaceutical companies, academic institutions, government agencies and other public and private research organizations. Many of these competitors, either alone or together with their collaborative partners, operate larger research and development programs or have substantially greater financial resources than we do, as well as significantly greater experience in:

- developing drugs;

- undertaking nonclinical testing and human clinical studies;

- obtaining FDA and other regulatory approvals of drugs;

- formulating and manufacturing drugs; and

- launching, marketing and selling drugs.

We may not have or be able to obtain the same resources and experience as our competitors. If we are unable to perform these tasks effectively and efficiently, our results of operations might be materially adversely affected.

Developments by competitors might render our product candidates or technologies obsolete or non-competitive.

The pharmaceutical and biotechnology industries are intensely competitive. In addition, the clinical and commercial landscape for HBV, ulcerative colitis (UC), inflammatory bowel disease (IBD), including Crohn's disease, irritable bowel syndrome (IBS), immune-mediated and metabolic disorders and oncology is rapidly changing; we expect new data from commercial and clinical-stage products to continue to emerge. We will compete with organizations that have existing treatments and that are or will be developing treatments for the indications that our product candidates target. If our competitors develop effective treatments for HBV, UC, IBD, IBS, immune-mediated and metabolic disorders and oncology or any other indication or field we might pursue, and successfully commercialize those treatments, our business and prospects might be materially harmed, due to intense competition in these markets.

Companies with core inhibitor products or microbiome products may produce negative clinical data, which will adversely affect public perception of our product candidates, and may negatively impact regulatory approval of, or demand for, our potential products.

Negative data from clinical trials using core inhibitors or microbiome-based therapies (e.g., fecal transplant) could negatively impact the perception of the therapeutic use of our HBV or microbiome product candidates, respectively. This could negatively impact our ability to enroll patients in clinical trials. The clinical and commercial success of our potential products will depend in part on the public and clinical communities' acceptance of the use of core inhibitor product candidates and oral live microbial biotherapeutic products (LBPs). Moreover, our success depends upon physicians prescribing, and their patients being willing to receive, treatments that involve the use of core inhibitor product candidates or LBPs we may develop in lieu of, or in addition to, existing treatments with which they are already familiar and for which more clinical data may be available. Adverse events in our preclinical studies or clinical trials or those of our competitors or of academic researchers utilizing core inhibitor therapies or microbiome therapies, even if not ultimately attributable to our product candidates, and any resulting publicity could result in increased governmental regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our product candidates, stricter labeling requirements for our product candidates that are approved, if any, and a decrease in demand for any such products.

Our product candidates under development in our Microbiome program will be subject to regulation as biologics. These candidates, and any other future product candidates for which we or our collaborators intend to seek approval as biologic products, may face competition sooner than anticipated.

The ACA includes a subtitle called the Biologics Price Competition and Innovation Act of 2009 (BPCIA), which created an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years following the date that the reference product was first licensed by the FDA. In addition, the approval of a biosimilar product may not be made effective by the FDA until 12 years from the date on which the reference product was first licensed. During this 12-year period of exclusivity, another company may still market a competing version of the reference product if the FDA approves a full BLA for the competing product containing the sponsor's own preclinical data and data from adequate and well-controlled clinical studies to demonstrate the safety, purity and potency of their product. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when such processes intended to implement the BPCIA may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for our biological products.

We believe that if product candidates from our Microbiome program are approved as biological products under a BLA, they should qualify for the 12-year period of exclusivity. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider our product candidates to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

If we or our collaborators are not able to develop collaborative marketing relationships with licensees or partners, or create effective internal sales, marketing, and distribution capability, we might be unable to market our products successfully.

To market our product candidates, if approved, we will have to establish our own marketing and sales force or out-license our product candidates to, or collaborate with, larger firms with experience in marketing and selling pharmaceutical products. There can be no assurance that we will be able to successfully establish our own marketing capabilities or establish marketing, sales, or distribution relationships with third parties; that such relationships, if established, will be successful; or that we will be successful in gaining market acceptance for our product candidates. To the extent that we enter into any marketing, sales, or distribution arrangements with third parties, our product revenues will be lower than if we marketed and sold our products directly, and any revenues we receive will depend upon the efforts of such third parties. If we are unable to establish such third-party sales and marketing relationships, or choose not to do so, we will have to establish our own in-house capabilities. We, as a company, have no experience in marketing or selling pharmaceutical products and currently have no sales, marketing, or distribution infrastructure. To market any of our products directly, we would need to develop a marketing, sales, and distribution force that both has technical expertise and the ability to support a distribution capability. To establish our own marketing, sales, and distribution capacity would significantly increase our costs, and require substantial additional capital. In addition, there is intense competition for proficient sales and marketing personnel, and we might not be able to attract individuals who have the qualifications necessary to market, sell, and distribute our products. There can be no assurance that we will be able to establish internal marketing, sales, or distribution capabilities.

The commercial success of our product candidates will depend upon the degree of market acceptance by physicians, patients, third-party payors and others in the medical community.

The commercial success of our products, if approved for marketing, will depend in part on the medical community, patients and third-party payors accepting our product candidates as effective and safe. If these products do not achieve an adequate level of acceptance, we may not generate significant product revenue and may not become profitable. The degree of market acceptance of our products, if approved for marketing, will depend on a number of factors, including:

- the actual or perceived safety and efficacy of the products, and advantages over alternative treatments;
- the pricing and cost-effectiveness of our products relative to competing products or therapies, including generic drugs or biosimilars, if available;
- the labeling of any approved product;
- the prevalence and severity of any side effects, including any limitations or warnings contained in a product's approved labeling;
- the emergence, and timing of market introduction, of competitive products;
- the effectiveness of marketing and distribution efforts by us and our licensees and distributors, if any; and
- the availability of third-party insurance coverage or governmental reimbursement.

Even if a potential product displays a favorable efficacy and safety profile in nonclinical studies and clinical studies, market acceptance of the product will not be known until after it is launched. Any failure to achieve market acceptance for our product candidates will harm our business, results and financial condition.

If we lose key management or scientific personnel, cannot recruit qualified employees, officers, or other significant personnel or experience increases in our compensation costs, our business might materially suffer.

We are highly dependent on the services of our executive officers and senior management team. Our employment agreements with our executive officers and senior management team members do not ensure their retention.

Furthermore, our future success also depends, in part, on our ability to identify, hire, and retain additional management team members as our operations grow and our ability to replace our management team members in the event any leave us for any reason. We expect to experience intense competition for qualified personnel and might be unable to attract and retain the personnel necessary for the development of our business. Finally, we do not currently

maintain, nor do we intend to obtain in the future, "key man" life insurance that would compensate us in the event of the death or disability of any of the members of our management team.

The failure by us to retain, attract and motivate executives and other key employees could have a material adverse impact on our business, financial condition and results of operations.

If we are unable to hire and retain additional qualified personnel, our ability to grow our business might be harmed.

As of December 31, 2019, we had 115 employees and contracts with a number of temporary contractors, consultants and contract research organizations. We will need to hire or contract with additional qualified personnel with expertise in clinical research and testing, formulation and manufacturing and sales and marketing to commercialize our HBV drug candidates and our microbiome biotherapeutic candidates or any other product candidate we may seek to develop. We compete for qualified individuals with numerous biopharmaceutical companies, universities and other research institutions. Competition for these individuals is intense, and we cannot be certain that our search for such personnel will be successful. Attracting and retaining qualified personnel will be critical to our success, and any failure to do so could have a material adverse impact on our business, financial condition and results of operations.

Significant disruptions of information technology systems or breaches of data security could materially adversely affect our business, results of operations and financial condition.

We collect and maintain information in digital form that is necessary to conduct our business, and we are increasingly dependent on information technology systems and infrastructure to operate our business. In the ordinary course of our business, we collect, store and transmit large amounts of confidential information, including intellectual property, proprietary business information and personal information. It is critical that we do so in a secure manner to maintain the confidentiality and integrity of such confidential information. We have established physical, electronic and organizational measures to safeguard and secure our systems to prevent this data from being compromised, and we rely on commercially available systems, software, tools, and monitoring to provide security for our information technology systems and the processing, transmission and storage of digital information. We have also outsourced elements of our information technology infrastructure, and as a result, a number of third-party vendors may or could have access to our confidential information. Our internal information technology systems and infrastructure, and those of our current and any future collaborators, contractors and consultants and other third parties on which we rely, are vulnerable to damage from computer viruses, malware, natural disasters, terrorism, war, telecommunication and electrical failures, cyberattacks or cyber intrusions over the Internet, attachments to emails, persons inside our organization, or persons with access to systems inside our organization.

The risk of a security breach or disruption, particularly through cyberattacks or cyber intrusion, including by computer hackers, foreign governments and cyberterrorists, has generally increased as the number, intensity and sophistication of attempted attacks and intrusions from around the world have increased. In addition, the prevalent use of mobile devices that access confidential information increases the risk of data security breaches, which could lead to the loss of confidential information or other intellectual property. The costs to us to mitigate network security problems, bugs, viruses, worms, malicious software programs and security vulnerabilities could be significant, and while we have implemented security measures to protect our data and information technology systems, our efforts to address these problems may not be successful, and these problems could result in unexpected interruptions, delays, cessation of service and other harm to our business and our competitive position. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our product development programs. For example, the loss of clinical study data from completed or ongoing or planned clinical studies could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data.

Moreover, if a computer security breach affects our systems or results in the unauthorized release of personally identifiable information, our reputation could be materially damaged. In addition, such a breach may require notification to governmental agencies, the media or individuals pursuant to various federal, state and non-U.S. privacy and security laws, if applicable, including the Health Insurance Portability and Accountability Act of 1996 (HIPAA), as amended by the Health Information Technology for Clinical Health Act of 2009 (HITECH), and its implementing rules and regulations, as well as regulations promulgated by the Federal Trade Commission, state breach notification law and the European Union's General Data Protection Regulation (GDPR). We would also be exposed to a risk of loss or litigation and potential liability, which could materially adversely affect our business, results of operations and financial condition.

We might not successfully manage our growth.

Our success will depend upon the expansion of our operations and the effective management of our growth, which will place a significant strain on our current and future management and other administrative and operational resources. To manage this growth, we may need to expand our facilities, augment our operational, financial and management systems and hire and train additional qualified personnel. If we are unable to manage our growth effectively, our business would be harmed.

We might seek to develop our business through acquisitions of or investment in new or complementary businesses, products or technologies, and the failure to manage these acquisitions or investments, or the failure to integrate them with our existing business, could have a material adverse effect on us.

We might consider opportunities to acquire or invest in other technologies, products and businesses that might enhance our capabilities or complement our current product candidates. Potential and completed acquisitions and strategic investments involve numerous risks, including potential problems or issues associated with the following:

- assimilating the acquired technologies, products or business operations;
- maintaining uniform standards, procedures, controls and policies;
- unanticipated costs associated with the acquisition or investment;
- diversion of our management's attention from our preexisting business;
- maintaining or obtaining the necessary regulatory approvals or complying with regulatory requirements; and
- adverse effects on existing business operations.

We have no current commitments with respect to any acquisition or investment in other technologies or businesses. We do not know if we will identify suitable acquisitions, whether we will be able to successfully complete any acquisitions, or whether we will be able to successfully integrate any acquired product, technology or business into our business or retain key personnel, suppliers or collaborators.

Our ability to develop successfully our business through acquisitions would depend on our ability to identify, negotiate, complete and integrate suitable target businesses or technologies and obtain any necessary financing. These efforts could be expensive and time consuming and might disrupt our ongoing operations. If we are unable to integrate efficiently any acquired business, technology or product into our business, our business and financial condition might be adversely affected.

Risks Related to Our Regulatory and Legal Environment

We are and will be subject to extensive and costly government regulation and the failure to comply with these regulations may have a material adverse effect on our operations and business.

Product candidates employing our technology are subject to extensive and rigorous domestic government regulation including regulation by the FDA, the Centers for Medicare and Medicaid Services, other divisions of the U.S. Department of Health and Human Services, the U.S. Department of Justice, state and local governments, and their respective foreign equivalents. Both before and after approval of any product, we and our collaborators, suppliers, contract manufacturers and clinical investigators are subject to extensive regulation by governmental authorities in the United States and other countries, covering, among other things, testing, manufacturing, quality control, clinical studies, post-marketing studies, labeling, advertising, promotion, distribution, import and export, governmental pricing, price reporting and rebate requirements. Failure to comply with applicable requirements could result in one or more of the following actions: warning or untitled letters; unanticipated expenditures; delays in approval or refusal to approve a product candidate; voluntary or mandatory product recall; product seizure; interruption of manufacturing or clinical studies; operating or marketing restrictions; injunctions; criminal prosecution and civil or criminal penalties including fines and other monetary penalties; exclusion from federal health care programs such as Medicare and Medicaid; adverse publicity; and disruptions to our business. Further, government investigations into potential violations of these laws would require us to expend considerable resources and face adverse publicity and the potential disruption of our business even if we are ultimately found not to have committed a violation. If products employing our technologies are marketed abroad, they will also be subject to extensive regulation by

foreign governments, whether or not they have obtained FDA approval for a given product and its uses. Such foreign regulation might be equally or more demanding than corresponding U.S. regulation.

Government regulation substantially increases the cost and risk of researching, developing, manufacturing, and selling our product candidates. The regulatory review and approval process, which includes nonclinical testing and clinical studies of each product candidate, is lengthy, expensive, and uncertain. We or our collaborators must obtain and maintain regulatory authorization to conduct clinical studies and approval for each product we intend to market, and the manufacturing facilities used for the products must be inspected and meet legal requirements. Securing regulatory approval requires submitting extensive nonclinical and clinical data and other supporting information for each proposed therapeutic indication in order to establish the product's safety and efficacy for each intended use. The development and approval process might take many years, requires substantial resources, and might never lead to the approval of a product.

Even if we or our collaborators are able to obtain regulatory approval for a particular product, the approval might limit the intended medical uses for the product, limit our ability to promote, sell, and distribute the product, require that we conduct costly post-marketing surveillance, and/or require that we conduct ongoing post-marketing studies. Material changes to an approved product, such as, for example, manufacturing changes or revised labeling, might require further regulatory review and approval. Once obtained, any approvals might be withdrawn, including, for example, if there is a later discovery of previously unknown problems with the product, such as a previously unknown safety issue.

If we, our collaborators, or our contract manufacturers fail to comply with applicable regulatory requirements at any stage during the regulatory process, such noncompliance could result in, among other things, delays in the approval of applications or supplements to approved applications; refusal by a regulatory authority, including the FDA, to review pending market approval applications or supplements to approved applications; untitled letters or warning letters; fines; import and export restrictions; product recalls or seizures; injunctions; total or partial suspension of production; civil penalties; withdrawals of previously approved marketing applications; recommendations by the FDA or other regulatory authorities against governmental contracts; and/or criminal prosecutions.

The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming and inherently unpredictable, and if we or our collaborators are ultimately unable to obtain regulatory approval for our product candidates, our business will be substantially harmed.

We, or any current or future collaborators, cannot assure you that we will receive the approvals necessary to commercialize for sale any of our product candidates, or any product candidate we acquire or develop in the future. We will need FDA approval to commercialize our product candidates in the United States and approvals from the applicable regulatory authorities in foreign jurisdictions to commercialize our product candidates in those jurisdictions. In order to obtain FDA approval of any product candidate, we must submit to the FDA an NDA, in the case of our HBV Cure program, or a BLA, in the case of our product candidates in our Microbiome program, demonstrating that the product candidate is safe for humans and effective for its intended use (for biological products, this standard is referred to as safe, pure and potent). This demonstration requires significant research, nonclinical studies, and clinical studies. Satisfaction of the FDA's regulatory requirements typically takes many years, depends upon the type, complexity and novelty of the product candidate and requires substantial resources for research, development and testing. We cannot predict whether our research and clinical approaches will result in drugs or biological products that the FDA considers safe for humans and effective for their indicated uses. The FDA has substantial discretion in the approval process and might require us to conduct additional nonclinical and clinical testing, perform post-marketing studies or otherwise limit or impose conditions on any approval we obtain.

The approval process might also be delayed by changes in government regulation, future legislation or administrative action or changes in FDA policy that occur prior to or during our regulatory review. Delays in obtaining regulatory approvals might:

- delay commercialization of, and our ability to derive product revenues from, our product candidates;
- impose costly procedures on us; and
- diminish any competitive advantages that we might otherwise enjoy.

Even if we comply with all FDA requests, the FDA might ultimately reject one or more of our NDAs or BLAs. We cannot be sure that we will ever obtain regulatory approval for our product candidates. Failure to obtain FDA approval of our product candidates will severely undermine our business by leaving us without a saleable product, and therefore without any source of revenues, until another product candidate could be developed or obtained. There is no guarantee that we will ever be able to develop an existing, or acquire another, product candidate.

In foreign jurisdictions, we must receive approval from the appropriate regulatory authorities before we can commercialize any product candidates. The risks associated with foreign regulatory approval processes are similar to the risks associated with the FDA approval procedures described above. We cannot assure you that we will receive the approvals necessary to commercialize our product candidates for sale outside the United States.

Even if our product candidates are approved, we and our collaborators will be subject to extensive post-approval regulation, including ongoing obligations and continued regulatory review, which may result in significant additional expense. If approved, our product candidates could be subject to post-marketing restrictions or withdrawal from the market and we, or any collaborators, may be subject to substantial penalties if we, or they, fail to comply with regulatory requirements or if we, or they, experience unanticipated problems with our products following approval.

Once a product candidate is approved, numerous post-approval requirements apply. Among other things, we and our collaborators will be subject to requirements regarding testing, manufacturing, quality control, clinical studies, post-marketing studies, labeling, advertising, promotion, distribution, import and export, governmental pricing, price reporting and rebate requirements. The holder of an approved NDA or BLA is subject to ongoing FDA oversight, monitoring and reporting obligations, including obligations to monitor and report adverse events and instances of the failure of a product to meet the specifications in the NDA or BLA. Application holders must submit new or supplemental applications and obtain FDA approval for changes to the approved product, product labeling, or manufacturing process, depending on the nature of the change. Application holders also must submit advertising and other promotional material to the FDA and report on ongoing clinical studies. The FDA also has the authority to require changes in the labeling of approved drug products and to require post-marketing studies. The FDA can also impose distribution and use restrictions under a REMS.

Advertising and promotional materials must comply with FDA rules in addition to other applicable federal and state laws. The distribution of product samples to physicians must comply with the requirements of the Prescription Drug Marketing Act. Manufacturing facilities remain subject to FDA inspection and must continue to adhere to the FDA's cGMP requirements. Sales, marketing, and scientific/educational grant programs, among other activities, must comply with the anti-fraud and abuse provisions of the Social Security Act, the False Claims Act, and similar state laws, each as amended. Pricing and rebate programs must comply with the Medicaid rebate requirements of the Omnibus Budget Reconciliation Act of 1990 and the Veterans Health Care Act of 1992, each as amended. If products are made available to authorized users of the Federal Supply Schedule of the General Services Administration, additional laws and requirements apply. All of these activities are also potentially subject to federal and state consumer protection and unfair competition laws.

Depending on the circumstances, failure to meet these post-approval requirements can result in criminal prosecution, fines, injunctions, recall or seizure of products, total or partial suspension of production, denial or withdrawal of pre-marketing product approvals, license revocation or refusal to allow us to enter into supply contracts, including government contracts. In addition, even if we comply with FDA and other requirements, new information regarding the safety or effectiveness of a product could lead the FDA to modify or withdraw product approval or revise product labeling.

The policies of the FDA and of other regulatory authorities may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, certain policies of the current administration may impact our business and industry. Namely, the current administration has taken several executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, FDA's ability to engage in routine oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. Notably, on January 30, 2017, an Executive Order was issued directing all executive agencies, including the FDA, that, for each notice of proposed rulemaking or final regulation to be issued in fiscal years 2018 and beyond, the agencies must identify regulations to

offset any incremental cost of a new regulation. On September 8, 2017, the FDA published notices in the Federal Register soliciting broad public comment to identify regulations that could be modified in compliance with this Executive Order. It is difficult to predict how these requirements will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose restrictions on FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted. In addition, if we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability.

Even if we or our collaborators are able to commercialize any product candidates, those products may become subject to unfavorable pricing regulations, third-party coverage and reimbursement practices or healthcare reform initiatives, which would harm our business.

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

We have never commercialized a product, and even if any product candidate of ours is approved by the appropriate regulatory authorities for marketing and sale, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. Physicians may be reluctant to take their patients off their current medications and switch their treatment regimen. Further, patients often acclimate to the treatment regime that they are currently taking and do not want to switch unless their physicians recommend switching products or they are required to switch due to lack of coverage and adequate reimbursement. In addition, even if we are able to demonstrate our product candidates' safety and efficacy to the FDA and other regulators, safety or efficacy concerns in the medical community may hinder market acceptance.

Efforts to educate the medical community and third-party payors on the benefits of our product candidates may require significant resources, including management time and financial resources, and may not be successful. If any of our product candidates are approved but do not achieve an adequate level of market acceptance, we may not generate significant revenues and we may not become profitable. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and safety of the product;
- the potential advantages of the product compared to competitive therapies;
- the prevalence and severity of any side effects;
- whether the product is designated under physician treatment guidelines as a first-, second- or third-line therapy;
- our ability, or the ability of any future collaborators, to offer the product for sale at competitive prices;
- the product's convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try, and of physicians to prescribe, the product;
- limitations or warnings, including distribution or use restrictions contained in the product's approved labeling;

- the strength of sales, marketing and distribution support;
- changes in the standard of care for the targeted indications for the product; and
- availability and adequacy of coverage and reimbursement from government payors, managed care plans and other third-party payors.

Our ability to commercialize any medicines successfully also will depend in part on the extent to which reimbursement for these medicines and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any product candidate that we commercialize and, if reimbursement is available, the level of reimbursement. Reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If reimbursement is not available or is available only to limited levels, we may not be able to commercialize successfully any product candidate for which we obtain marketing approval.

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

In the United States and in other countries, there have been, and we expect there will continue to be, a number of legislative and regulatory proposals to change the healthcare system in ways that could significantly affect our business. International, federal and state lawmakers regularly propose and, at times, enact legislation that would result in significant changes to the healthcare system, some of which are intended to contain or reduce the costs of medical products and services. The U.S. government and other governments have shown significant interest in pursuing healthcare reform, as evidenced by the ACA.

Among the provisions of the ACA of importance to our potential drug candidates are the following:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologics;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- expansion of healthcare fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, new government investigative powers, and enhanced penalties for noncompliance;

- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices (which was increased to 70% as of January 1, 2019 under the Bipartisan Budget Act of 2018 (BBA));

- extension of manufacturers' Medicaid rebate liability;

- expansion of eligibility criteria for Medicaid programs;

- expansion of the entities eligible for discounts under the Public Health Service Act pharmaceutical pricing program;

- new requirements to report financial arrangements with physicians and teaching hospitals;

- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and

- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

Since its enactment, there have been many judicial, Presidential, and Congressional challenges to numerous aspects of the ACA, and the long ranging effects of these challenges on reimbursement by third-party payors, the viability of the ACA marketplace, providers, and potentially, our business are unknown at this time. In addition, the full impact of the ACA, any law repealing and/or replacing elements of it, and the political uncertainty surrounding any repeal or replacement legislation on our business remains unclear.

Further, in some foreign jurisdictions, there have been a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our products profitably. The continuing efforts of U.S. and other governments, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce healthcare costs may adversely affect our ability to set satisfactory prices for our products, to generate revenues from the sale of products, and to achieve and maintain profitability.

We and our collaborators may be subject, directly or indirectly, to applicable U.S. federal and state anti-kickback, false claims laws, physician payment transparency laws, fraud and abuse laws or similar healthcare and security laws and regulations, and health information privacy and security laws, which could expose us or them to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and others play a primary role in the recommendation and prescription of any products for which we obtain regulatory approval. If we obtain FDA approval for any of our drug candidates and begin commercializing those drugs in the United States, our operations may be subject to various federal and state fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute, the federal False Claims Act, and physician payment sunshine laws and regulations. Additionally, we are subject to state and non-U.S. equivalents of each of the healthcare laws described above, among others, some of which may be broader in scope and may apply regardless of the payor. These laws may impact, among other things, our proposed sales, marketing and education programs. In addition, we may be subject to patient privacy regulation by both the federal government and the states and foreign jurisdictions in which we conduct our business. There are ambiguities as to what is required to comply with these requirements, and if we fail to comply with any applicable federal, state or foreign legal requirement, we could be subject to penalties.

Regulators globally are imposing greater monetary fines for privacy violations. The GDPR, which went into effect on May 25, 2018, applies to any company established in the European Union (EU) as well as to those outside the EU if they collect and use personal data in connection with the offering goods or services to individuals in the EU or the monitoring of their behavior. The GDPR enhances data protection obligations for processors and controllers of personal data, including, for example, expanded disclosures about how personal information is to be used, limitations on retention of information, mandatory data breach notification requirements and onerous new obligations on services providers. Noncompliance with the GDPR may result in monetary penalties of up to €20 million or 4% of worldwide revenue, whichever is higher. The GDPR may increase our responsibility and liability in

relation to personal data that we process where such processing is subject to the GDPR, and we may be required to put in place additional mechanisms to ensure compliance with the GDPR, including as implemented by individual countries. Compliance with the GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of personal data, such as healthcare data or other sensitive information, could greatly increase our cost of developing our products and services or even prevent us from offering certain products in jurisdictions that we may operate in. Given the limited enforcement of the GDPR to date, particularly in the pharmaceutical space, we face uncertainty as to the exact interpretation of the new requirements on our trials and we may be unsuccessful in implementing all measures required by data protection authorities or courts in interpretation of the new law.

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

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. In addition, recent health care reform legislation has strengthened these laws. For example, the ACA, among other things, amends the intent requirement of the federal Anti-Kickback and criminal healthcare fraud statutes. As a result of such amendment, a person or entity no longer needs to have actual knowledge of these statutes or specific intent to violate them in order to have committed a violation. Moreover, the ACA provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

Violations of fraud and abuse laws may be punishable by criminal and/or civil sanctions, including penalties, fines and/or exclusion or suspension from federal and state healthcare programs such as Medicare and Medicaid and debarment from contracting with the U.S. government. In addition, private individuals have the ability to bring actions on behalf of the U.S. government under the federal False Claims Act as well as under the false claims laws of several states.

Law enforcement authorities are increasingly focused on enforcing fraud and abuse laws, and it is possible that some of our practices may be challenged under these laws. Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, disgorgement, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations. In addition, the approval and commercialization of any of our drug candidates outside the United States will also likely subject us to non-U.S. equivalents of the healthcare laws mentioned above, among other non-U.S. laws.

If any of the physicians or other providers or entities with whom we expect to do business with are found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs, which may also adversely affect our business.

If we fail to maintain an effective system of disclosure controls and internal control over financial reporting, our ability to produce timely and accurate financial statements or comply with applicable regulations could be impaired.

The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting. We are continuing to refine our disclosure controls and other procedures that are designed to ensure that the information that we are required to disclose in the reports that we will file with the SEC is properly recorded, processed, summarized and reported within the time periods specified in SEC rules and forms. We are also continuing to improve our internal control over financial reporting. We have expended, and anticipate that we will continue to expend, significant resources in order to maintain and improve the effectiveness of our disclosure controls and procedures and internal control over financial reporting.

Our current controls and any new controls that we develop in the future may become inadequate because of changes in conditions in our business. Further, weaknesses in our disclosure controls or our internal control over financial reporting may be discovered in the future. Any failure to develop or maintain effective controls, or any difficulties encountered in their implementation or improvement, could harm our operating results or cause us to fail to meet our reporting obligations and may result in a restatement of our financial statements for prior periods. Any failure to implement and maintain effective internal control over financial reporting could also adversely affect the results of management reports and independent registered public accounting firm audits of our internal control over financial reporting that we will be required to include in our periodic reports that will be filed with the SEC. If we were to have ineffective disclosure controls and procedures or internal control over financial reporting, our investors could lose confidence in our reported financial and other information, which would likely have a negative effect on the market price of our common stock.

We face the risk of product liability claims and might not be able to obtain insurance.

Our business exposes us to the risk of product liability claims that are inherent in the development of drugs and biotherapeutics. If the use of one or more of our product candidates or approved drugs, if any, harms people, we might be subject to costly and damaging product liability claims brought against us by clinical study participants, consumers, health care providers, pharmaceutical companies or others selling our products. Our inability to obtain sufficient product liability/clinical study insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of pharmaceutical products we develop. We cannot predict all of the possible harms or side effects that might result and, therefore, the amount of insurance coverage we maintain might not be adequate to cover all liabilities we might incur. We intend to expand our insurance coverage to include product liability insurance covering the sale of commercial products if we obtain marketing approval for our drug candidates in development, but we might be unable to obtain commercially reasonable product liability insurance for any products approved for marketing. If we are unable to obtain insurance at an acceptable cost or otherwise protect against potential product liability claims, we will be exposed to significant liabilities, which might materially and adversely affect our business and financial position. If we are sued for any injury allegedly caused by our products, our liability could exceed our total assets and our ability to pay the liability. Any successful product liability claims or series of claims brought against us would decrease our cash and could cause the value of our common stock to decrease.

We might be exposed to liability claims associated with the use of hazardous materials and chemicals.

Our research, development and manufacturing activities and/or those of our third-party contractors might involve the controlled use of hazardous materials and chemicals. Although we will strive to have our safety procedures, and those of our contractors, for using, storing, handling and disposing of these materials comply with federal, state and local laws and regulations, we cannot completely eliminate the risk of accidental injury or contamination from these materials. In the event of such an accident, we could be held liable for any resulting damages, and any liability could materially adversely affect our business, financial condition and results of operations. In addition, the federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of hazardous or radioactive materials and waste products might require us to incur substantial compliance costs that could materially adversely affect our business, financial condition and results of operations. We currently do not carry hazardous materials liability insurance. We intend to obtain such insurance in the future, if necessary, but cannot give assurance that we could obtain such coverage.

Our employees, independent contractors, consultants, collaborators and contract research organizations may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could result in significant liability for us and harm our reputation.

We are exposed to the risk of fraud or other misconduct, including intentional failure to:

- comply with FDA regulations or similar regulations of comparable foreign regulatory authorities;
- provide accurate information to the FDA or comparable foreign regulatory authorities;
- comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities;
- comply with the United States Foreign Corrupt Practices Act (the FCPA), the U.K. Bribery Act 2010, the PRC Criminal Law, the PRC Anti-unfair Competition Law and other anti-bribery laws;
- report financial information or data accurately; or
- disclose unauthorized activities to us.

Misconduct could also involve the improper use or misrepresentation of information obtained in the course of clinical studies, creating fraudulent data in our nonclinical studies or clinical studies or illegal misappropriation of product materials, which could result in regulatory sanctions, delays in clinical studies, or serious harm to our reputation. We have adopted a code of conduct for our directors, officers and employees (the Code of Conduct), but it is not always possible to identify and deter employee misconduct. The precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us and we are not successful in defending ourselves or asserting our rights, those actions could harm our business, results of operations, financial condition and cash flows, including through the imposition of significant fines or other sanctions.

We are subject to certain U.S. and foreign anti-corruption, anti-money laundering, export control, sanctions, and other trade laws and regulations (collectively, Trade Laws). We can face serious consequences for violations.

Among other matters, Trade Laws prohibit companies and their employees, agents, clinical research organizations, legal counsel, accountants, consultants, contractors, and other partners from authorizing, promising, offering, providing, soliciting, or receiving directly or indirectly, corrupt or improper payments or anything else of value to or from recipients in the public or private sector. Violations of Trade Laws can result in substantial criminal fines and civil penalties, imprisonment, the loss of trade privileges, debarment, tax reassessments, breach of contract and fraud litigation, reputational harm, and other consequences. We have direct or indirect interactions with officials and employees of government agencies or government-affiliated hospitals, universities, and other organizations. We also expect our non-U.S. activities, particularly in China, to increase in time. We engage third parties for clinical studies and/or to obtain necessary permits, licenses, patent registrations, and other regulatory approvals. We can be held liable for the corrupt or other illegal activities of our personnel, agents, or partners, even if we do not explicitly authorize or have prior knowledge of such activities.

We have international operations, including in China, and conduct clinical studies outside of the United States. A number of risks associated with international operations could materially and adversely affect our business.

We could be subject to a number of risks related with our international operations, many of which may be beyond our control. These risks include:

- different regulatory requirements for drug approvals in foreign countries;
- different standards of care in various countries that could complicate the evaluation of our product candidates;
- different U.S. and foreign drug import and export rules;

- different reimbursement systems and different competitive drugs indicated to treat the indication for which our product candidates are being developed;
- reduced protection for intellectual property rights in certain countries;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- compliance with the FCPA and other anti-corruption and anti-bribery laws;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations and compliance with foreign currency exchange rules, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country; and
- business interruptions resulting from geopolitical actions, including tariffs, war and terrorism, natural disasters or outbreaks of disease, such as the outbreak of the novel strain of coronavirus (COVID-19) impacting China and elsewhere.

Certain of our clinical trials and manufacturing of our drug candidates take place in China through third-party CROs, collaborators or manufacturers. A significant disruption in the operation of those CROs, collaborators or manufacturers, could materially adversely affect our business, financial condition and results of operations.

We rely on certain third parties located in China to manufacture our drug candidates. In addition, we are conducting clinical studies in China through CROs located in China and we expect to conduct other clinical studies in China in the future. A natural disaster, epidemic or pandemic disease outbreaks, including the recent COVID-19 outbreak or other events could (i) significantly disrupt the business or operations of our CROs, manufacturers and the clinical sites conducting our clinical studies, (ii) impact clinical study recruitment and enrollment, affect compliance with clinical study protocols and/or impair the ability of sites to monitor enrolled patients, and (iii) delay regulatory filings and interactions with China regulatory agencies. To date, the COVID-19 outbreak has not caused significant disruptions in our manufacturing and clinical studies in China or elsewhere. We will continue to monitor the effects of the COVID-19 outbreak in China and elsewhere on our current and planned clinical studies. Any disruption in China that significantly services provided by CROs for our research and development programs, clinical trial operations conducted by CROs, or our manufacturers' ability to produce certain drug product candidates in adequate quantities to meet our needs could impede, delay, limit or prevent the research and development of our product candidates. The resulting impact on our research and development programs could materially adversely affect our business, financial condition and results of operations.

Risks Related to Our Intellectual Property

Our business depends on protecting our intellectual property.

If we and our licensors, IURTC and Therabiome, do not obtain protection for our respective intellectual property rights, our competitors might be able to take advantage of our research and development efforts to develop competing drugs. Our success, competitive position and future revenues, if any, depend in part on our ability and the abilities of our licensors to obtain and maintain patent protection for our products, methods, processes and other technologies, to preserve our trade secrets, to prevent third parties from infringing on our proprietary rights and to operate without infringing the proprietary rights of third parties.

We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies and chemical and biological compositions that are important to our business. To date, we and our licensors have filed patent applications intended to cover our products candidates and their methods of use. Although we co-own and have in-licensed two issued patents in the U.S. directed to compositions of matter that includes 731, which are expected to expire in 2035 and 2036, and we have in-licensed issued U.S. patents related to delivery technology for our Microbiome program, which are expected to expire in 2034, we do not own or have any rights to any issued patents that cover any of our other product candidates, and we cannot be certain that we will secure any rights to any issued patents with claims that cover any of our proprietary product candidates and technologies. The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible

that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection.

The patent process also is subject to numerous risks and uncertainties, and there can be no assurance that we will be successful in protecting our products by obtaining and defending patents. These risks and uncertainties include the following:

- Any patent rights, if obtained, might be challenged, invalidated, or circumvented, or otherwise might not provide any competitive advantage;

- Our competitors, many of which have substantially greater resources than we do and many of which might make significant investments in competing technologies, might seek, or might already have obtained, patents that will limit, interfere with, or eliminate our ability to make, use, and sell our potential products either in the United States or in international markets;

- As a matter of public policy regarding worldwide health concerns, there might be significant pressure on the U.S. government and other international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful; and

- Countries other than the United States might have patent laws that provide less protection than those governing U.S. courts, allowing foreign competitors the ability to exploit these laws to create, develop, and market competing products.

In addition, the U.S. Patent and Trademark Office (the USPTO) and patent offices in other jurisdictions have often required that patent applications concerning pharmaceutical and/or biotechnology-related inventions be limited or narrowed substantially to cover only the specific innovations exemplified in the patent application, thereby limiting the scope of protection against competitive challenges. Thus, even if we or our licensors are able to obtain patents, the patents might be substantially narrower than anticipated.

Patent and other intellectual property protection is crucial to the success of our business and prospects, and there is a substantial risk that such protections, if obtained, will prove inadequate. Our business and prospects will be harmed if we fail to obtain these protections or they prove insufficient.

If we fail to comply with our obligations under our license agreements, we could lose rights to our product candidates or key technologies.

We have obtained rights to develop, market and sell some of our product candidates and technologies through intellectual property license agreements with third parties, including IURTC and Therabiome. These license agreements impose various diligence, milestone payment, royalty and other obligations on us. If we fail to comply with our obligations under our license agreements, we could lose some or all of our rights to develop, market and sell products covered by these licenses, and our ability to form collaborations or partnerships may be impaired. In addition, disputes may arise under our license agreements with third parties, which could prevent or impair our ability to maintain our current licensing arrangements on acceptable terms and to develop and commercialize the affected product candidates.

We may incur substantial costs as a result of litigation or other proceedings relating to patent and other intellectual property rights.

If we choose to go to court to stop another party from using the inventions claimed in any patents we obtain, that individual or company has the right to ask the court to rule that such patents are invalid or should not be enforced against that third party. These lawsuits are expensive and would consume time and resources and divert the attention of managerial and scientific personnel even if we were successful in stopping the infringement of such patents. There is a risk that the court will decide that such patents are not valid and that we do not have the right to stop the other party from using the inventions. There is also the risk that, even if the validity of such patents is upheld, the court will refuse to stop the other party on the ground that such other party's activities do not infringe our rights to such patents. If we were not successful in defending our intellectual property, our competitors could develop and market products based on our discoveries, which may reduce demand for our products.

We rely on trade secret protections through confidentiality agreements with our employees, collaborators and other parties, and the breach of these agreements could adversely affect our business and prospects.

We rely on trade secrets and proprietary know-how, which we seek to protect, in part, through confidentiality, invention, and nondisclosure agreements with our employees, scientific advisors, consultants, collaborators, suppliers, and other parties. There can be no assurance that these agreements will not be breached, that we would have adequate remedies for any such breach or that our trade secrets will not otherwise become known to or independently developed by our competitors. If any of these events occurs, or we otherwise lose protection for our trade secrets or proprietary know-how, the value of this information may be greatly reduced.

If our employees or consultants breach their confidentiality obligations, to be able to enforce these confidentiality provisions, we would need to know of the breach and have sufficient funds to enforce the provisions. We cannot assure you that we would know of or be able to afford enforcement of any breach. In addition, such provisions are subject to state law and interpretation by courts, which could limit the scope and duration of these provisions. Any limitation on or non-enforcement of these confidentiality provisions could have an adverse effect on our business.

We may infringe the intellectual property rights of others, which may prevent or delay our product development efforts and stop us from commercializing or increase the costs of commercializing our product candidates.

Our success will depend in part on our ability to operate without infringing the proprietary rights of third parties. Our competitors may have filed, and may in the future file, patent applications covering products and technologies similar to ours. Any such patent application may have priority over our patent applications, which could further require us to obtain rights from third parties to issued patents covering such products and technologies. We cannot guarantee that the manufacture, use or marketing of any product candidates that we develop will not infringe third-party patents.

A third party may claim that we are using inventions covered by the third party's patent rights and may go to court to stop us from engaging in our normal operations and activities, including making or selling our product candidates. Patent litigation is costly and time consuming. We may not have sufficient resources to address these actions, and such actions could affect our results of operations and divert the attention of managerial and scientific personnel.

If a patent infringement suit were brought against us, we may be forced to stop or delay developing, manufacturing, or selling potential products that are claimed to infringe a third party's intellectual property, unless that third party grants us rights to use its intellectual property. In such cases, we may be required to obtain licenses to patents or proprietary rights of others in order to continue development, manufacture or sale of our products. If we are unable to obtain a license or develop or obtain non-infringing technology, or if we fail to defend an infringement action successfully, or if we are found to have infringed a valid patent, we may incur substantial monetary damages, encounter significant delays in bringing our product candidates to market and be precluded from manufacturing or selling our product candidates, any of which could harm our business significantly.

If our efforts to protect our proprietary technologies are not adequate, we may not be able to compete effectively in our market.

We rely upon a combination of patents, trade secret protection and contractual arrangements to protect the intellectual property related to our technologies. We will only be able to protect our products and proprietary information and technology by preventing unauthorized use by third parties to the extent that our patents, trade secrets, and contractual position allow us to do so. Any disclosure to or misappropriation by third parties of our trade secrets or confidential information could compromise our competitive position. Moreover, we may in the future be involved in legal or administrative proceedings involving our intellectual property initiated by third parties, and which proceedings can result in significant costs and commitment of management time and attention. As our product candidates continue in development, third parties may attempt to challenge the validity and enforceability of our patents and proprietary information and technologies.

We may in the future be involved in initiating legal or administrative proceedings involving the product candidates and intellectual property of our competitors. These proceedings can result in significant costs and commitment of management time and attention, and there can be no assurance that our efforts would be successful in preventing or limiting the ability of our competitors to market competing products.

Composition-of-matter patents relating to the active pharmaceutical ingredient (API) are generally considered to be the strongest form of intellectual property protection for pharmaceutical products. Such patents provide protection not limited to any one method of use. Method-of-use patents protect the use of a product for the specified method(s), and do not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. We rely on a combination of these and other types of patents to protect our product candidates, and there can be no assurance that our intellectual property will create and sustain the competitive position of our product candidates.

Biotechnology and pharmaceutical product patents involve highly complex legal and scientific questions and can be uncertain. Any patent applications that we own or license may fail to result in issued patents. Even if patents do successfully issue from our applications, third parties may challenge their validity or enforceability, which may result in such patents being narrowed, invalidated, or held unenforceable. Even if our patents and patent applications are not challenged by third parties, those patents and patent applications may not prevent others from designing around our claims and may not otherwise adequately protect our product candidates. If the breadth or strength of protection provided by the patents and patent applications we hold with respect to our product candidates is threatened, competitors with significantly greater resources could threaten our ability to commercialize our product candidates. Discoveries are generally published in the scientific literature well after their actual development, and patent applications in the United States and other countries are typically not published until 18 months after filing, and in some cases are never published. Therefore, we cannot be certain that we or our licensors were the first to make the inventions claimed in our owned and licensed patents or patent applications, or that we or our licensors were the first to file for patent protection covering such inventions. Subject to meeting other requirements for patentability, for U.S. patent applications filed prior to March 16, 2013, the first to invent the claimed invention is entitled to receive patent protection for that invention while, outside the United States, the first to file a patent application encompassing the invention is entitled to patent protection for the invention. The United States moved to a "first to file" system under the Leahy-Smith America Invents Act (AIA), effective March 16, 2013. The effects of this change and other elements of the AIA are currently unclear, as the USPTO is still implementing associated regulations, and the applicability of the AIA and associated regulations to our patents and patent applications have not been fully determined. This new system also includes new procedures for challenging issued patents and pending patent applications, which creates additional uncertainty. We may become involved in any variety of proceedings challenging our patents and patent applications or the patents and patent applications of others, and the outcome of any such proceedings are highly uncertain. An unfavorable outcome in any such proceedings could reduce the scope of, invalidate, and/or find our patent rights unenforceable, allowing third parties to commercialize our technology and compete directly with us, or result in our inability to manufacture, develop or commercialize our product candidates without infringing the patent rights of others. In addition to ongoing changes with the AIA and USPTO regulations, recent decisions of the Supreme Court of the United States, and the possibility of statutory change to patent subject matter eligibility law advocated by such groups as the Intellectual Property Owners Association and the American Intellectual Property Law Association, provide additional uncertainty.

In addition to the protection afforded by patents, we seek to rely on trade secret protection and confidentiality agreements to protect proprietary know-how, information, or technology that is not covered by our patents. Although our agreements require all of our employees to assign their inventions to us, and we require all of our employees, consultants, advisors and any third parties who have access to our trade secrets, proprietary know-how and other confidential information and technology to enter into appropriate confidentiality agreements, we cannot be certain that our trade secrets, proprietary know-how and other confidential information and technology will not be subject to unauthorized disclosure or that our competitors will not otherwise gain access to or independently develop substantially equivalent trade secrets, proprietary know-how and other information and technology. Furthermore, the laws of some foreign countries, in particular China, where we anticipate increasing our activity and commercializing our product candidates, 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 globally. If we are unable to prevent unauthorized disclosure of our intellectual property related to our product candidates and technology to third parties, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business and operations.

Our reliance on third parties and agreements with collaboration partners requires us to share our trade secrets, which increases the possibility that a competitor may discover them or that our trade secrets will be misappropriated or disclosed.

Our reliance on third-party contractors to develop and manufacture our product candidates is based upon agreements that limit the rights of the third parties to use or disclose our confidential information, including our trade secrets and know-how. Despite the contractual provisions, the need to share trade secrets and other confidential information increases the risk that such trade secrets and information are disclosed or used, even if unintentionally, in violation of these agreements. In the highly competitive markets in which our product candidates are expected to compete, protecting our trade secrets, including our strategies for addressing competing products, is imperative, and any unauthorized use or disclosure could impair our competitive position and may have a material adverse effect on our business and operations.

In addition, some of our collaboration partners are larger, more complex organizations than ours, and the risk of inadvertent disclosure of our proprietary information may be increased despite their internal procedures and contractual obligations in place with our collaboration partners. Despite our efforts to protect our trade secrets and other confidential information, a competitor's discovery of such trade secrets and information could impair our competitive position and have an adverse impact on our business.

We are developing an extensive worldwide patent portfolio. The cost of maintaining our patent protection is high and maintaining our patent protection requires continuous review and compliance in order to maintain worldwide patent protection. We may not be able to maintain effectively our intellectual property position throughout the major markets of the world.

The USPTO and foreign patent authorities require maintenance fees and payments as well as continued compliance with a number of procedural and documentary requirements. Noncompliance may result in abandonment or lapse of the subject patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Noncompliance may result in reduced royalty payments for lack of patent coverage in a particular jurisdiction from our collaboration partners or may result in competition, either of which could have a material adverse effect on our business.

We have made, and will continue to make, certain strategic decisions in balancing costs and the potential protection afforded by the patent laws of certain countries. As a result, we may not be able to prevent third parties from practicing our inventions in all countries throughout the world, or from selling or importing products made using our inventions in and into the United States or other countries. Third parties may use our technologies in territories in which we have not obtained patent protection to develop their own products and, further, may infringe our patents in territories which provide inadequate enforcement mechanisms, even if we have patent protection. Such third-party products may compete with our product candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

The laws of some foreign countries do not protect proprietary rights to the same extent as do the laws of the United States, and we may encounter significant problems in securing and defending our intellectual property rights outside the United States

Many companies have encountered significant problems in protecting and defending intellectual property rights in certain countries. The legal systems of certain countries, particularly countries such as China, do not always favor the enforcement of patents, trade secrets, and other intellectual property rights, particularly those relating to pharmaceutical and biotechnology products, which could make it difficult for us to stop infringement of our patents, misappropriation of our trade secrets, or marketing of competing products in violation of our proprietary rights. In China, our intended establishment of significant operations will depend in substantial part on our ability to enforce effectively our intellectual property rights in that country. Proceedings to enforce our intellectual property rights in foreign countries could result in substantial costs and divert our efforts and attention from other aspects of our business and could put our patents in these territories at risk of being invalidated or interpreted narrowly, or our patent applications at risk of not being granted and could provoke third parties to assert claims against us. We may not prevail in all legal or other proceedings that we may initiate and, if we were to prevail, the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Intellectual property rights do not address all potential threats to any competitive advantage we may have.

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

- Others may be able to make compounds that are the same as or similar to our current or future product candidates but that are not covered by the claims of the patents that we own or have exclusively licensed.
- We or any of our licensors or strategic partners might not have been the first to make the inventions covered by the issued patents or pending patent applications that we own or have exclusively licensed.
- We or any of our licensors or strategic partners might not have been the first to file patent applications covering certain of our inventions.
- Others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights.
- The prosecution of our pending patent applications may not result in granted patents.
- Granted patents that we own or have exclusively licensed may not provide us with any competitive advantages, or may be held invalid or unenforceable, as a result of legal challenges by our competitors.
- Patent protection on our product candidates may expire before we are able to develop and commercialize the product, or before we are able to recover our investment in the product.
- Our competitors might conduct research and development activities in the United States and other countries that provide a safe harbor from patent infringement claims for such activities, as well as in countries in which we do not have patent rights and may then use the information learned from such activities to develop competitive products for sale in markets where we intend to market our product candidates.

The existence of counterfeit pharmaceutical products in pharmaceutical markets may damage our brand and reputation and have a material adverse effect on our business, operations and prospects.

Counterfeit products, including counterfeit pharmaceutical products, are a significant problem, particularly in China. Counterfeit pharmaceuticals are products sold or used for research under the same or similar names, or similar mechanism of action or product class, but which are sold without proper licenses or approvals. The proliferation of counterfeit pharmaceuticals has grown in recent years and may continue to grow in the future. Such products may be used for indications or purposes that are not recommended or approved or for which there is no data or inadequate data with regard to safety or efficacy. Such products divert sales from genuine products, often are of lower cost, often are of lower quality (having different ingredients or formulations, for example), and have the potential to damage the reputation for quality and effectiveness of the genuine product. If counterfeit pharmaceuticals illegally sold or used for research result in adverse events or side effects to consumers, we may be associated with any negative publicity resulting from such incidents. Consumers may buy counterfeit pharmaceuticals that are in direct competition with our pharmaceuticals, which could have an adverse impact on our revenues, business and results of operations. In addition, counterfeit products could be used in nonclinical studies or clinical studies or could otherwise produce undesirable side effects or adverse events that may be attributed to our products as well, which could cause us or regulatory authorities to interrupt, delay or halt clinical studies and could result in the delay or denial of regulatory approval by the FDA or other regulatory authorities and potential product liability claims. With respect to China, although the government has recently been increasingly active in policing counterfeit pharmaceuticals, there is not yet an effective counterfeit pharmaceutical regulation control and enforcement system in China. As a result, we may not be able to prevent third parties from selling or purporting to sell our products in China. The existence of and any increase in the sales and production of counterfeit pharmaceuticals, or the technological capabilities of counterfeiters, could negatively impact our revenues, brand reputation, business and results of operations.

Risks Related to Our Common Stock

The price of our common stock might fluctuate significantly, and you could lose all or part of your investment.

Since our merger with Assembly Pharmaceuticals on July 11, 2014 through December 31, 2019, the closing price of our common stock has fluctuated widely. Continued volatility in the market price of our common stock might prevent a stockholder from being able to sell shares of our common stock at or above the price paid for such shares. The trading price of our common stock might be volatile and subject to wide price fluctuations in response to various factors, including:

- the progress, results and timing of our clinical studies and nonclinical studies and other studies involving our product candidates;
- success or failure of our product candidates;
- the receipt or loss of required regulatory approvals for our product candidates;
- availability of capital;
- future issuances by us of our common stock or securities exercisable for or convertible into common stock;
- sale of shares of our common stock by our significant stockholders or members of our management;
- additions or departures of key personnel;
- investor perceptions of us and the pharmaceutical industry;
- issuance of new or changed securities analysts' reports or recommendations, or the announcement of any changes to our credit rating;
- introduction of new products or announcements of significant contracts, acquisitions or capital commitments by us or our competitors;
- threatened or actual litigation and government investigations;
- legislative, political or regulatory developments;
- the overall performance of the equity markets;
- actual or anticipated fluctuations in our quarterly financial and operating results;
- general economic conditions;
- changes in interest rates; and
- changes in accounting standards, policies, guidance, interpretations or principles.

These and other factors might cause the market price of our common stock to fluctuate substantially, which might limit or prevent investors from readily selling their shares of our common stock and might otherwise negatively affect the liquidity of our common stock. In addition, in recent years, the stock market has experienced significant price and volume fluctuations. This volatility has had a significant impact on the market price of securities issued by many companies across many industries. The changes frequently appear to occur without regard to the operating performance of the affected companies. Accordingly, the price of our common stock could fluctuate based upon factors that have little or nothing to do with our company, and these fluctuations could materially reduce our share price.

We might not be able to maintain the listing of our common stock on the Nasdaq Global Select Market.

Our common stock is listed on the Nasdaq Global Select Market under the symbol "ASMB." We might not be able to maintain the listing standards of that exchange. If we fail to maintain the listing requirements, our common stock might trade on the OTC Bulletin Board or in the "pink sheets" maintained by OTC Markets Group Inc. These alternative markets are generally considered to be markets that are less efficient and less broad than the Nasdaq Global Select Market. A delisting of our common stock from the Nasdaq Global Select Market and our inability to list the stock on another national securities exchange could negatively impact us by: (i) reducing the liquidity and market price of our common stock; (ii) reducing the number of investors willing to hold or acquire our common stock, which could negatively impact our ability to raise equity financing; (iii) limiting our ability to use a registration statement to offer and sell freely tradable securities, thereby preventing us from accessing the public capital markets and (iv) impairing our ability to provide equity incentives to our employees.

We may be subject to securities litigation, which is expensive and could divert management attention.

The market price of our common stock may be volatile, and in the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. We may be the target of this type of litigation in the future. Securities litigation against us could result in substantial costs and divert our management's attention from other business concerns, which could seriously harm our business.

Our ability to use our net operating loss and credit carryforwards to offset future taxable income may be subject to certain limitations.

At December 31, 2019, we had potentially utilizable gross Federal net operating loss carryforwards of approximately $297.6 million, State net operating loss carry-forwards of approximately $309.3 million, Federal and California research and development credit carry forwards of approximately $9.0 million and $5.3 million, respectively, which will begin to expire in 2027. Our ability to utilize our net operating loss and credit carryforwards is dependent upon our ability to generate taxable income in future periods and may be limited due to restrictions imposed on utilization of net operating loss and credit carryforwards under federal and state laws upon a change in ownership.

Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, a corporation that undergoes an "ownership change," is subject to annual limitations on its ability to use its pre-change net operating loss carryforwards (NOLs) and other pre-change tax attributes (such as research tax credits) to offset its post-change income or taxes. For these purposes, an ownership change generally occurs where the equity ownership of one or more stockholders or groups of stockholders who owns at least 5% of a corporation's stock increases its ownership by more than 50 percentage points over its lowest ownership percentage within a three-year period (calculated on a rolling basis). We have determined that an ownership change occurred in each of December 2010, January 2013 and October 2014. The result of these ownership changes is that approximately $40.0 million of our approximately $297.6 million of net operating losses will not be available to us to offset future taxable income. In addition, we may experience ownership changes in the future, some of which are outside our control. Accordingly, we may not be able to utilize a material portion of our net operating losses or credits. Limitations on our ability to utilize our net operating losses to offset U.S. federal taxable income could potentially result in increased future tax liability to us. In addition, at the state level, there may be periods during which the use of net operating losses is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

Because U.S. federal net operating losses incurred in taxable periods beginning before January 1, 2018 generally may be carried forward for up to 20 years, the annual limitation may effectively provide a cap on the cumulative amount of pre-ownership change losses, including certain recognized built-in losses that may be utilized. Such pre-ownership change losses in excess of the cap may be lost. In addition, if an ownership change were to occur, it is possible that the limitations imposed on our ability to use pre-ownership change losses and certain recognized built-in losses could cause a net increase in our U.S. federal income tax liability and require U.S. federal income taxes to be paid earlier than otherwise would be paid if such limitations were not in effect. Further, if for financial reporting purposes the amount or value of these deferred tax assets is reduced, such reduction would have a negative impact on the book value of our common stock.

In addition, under the Tax Act, the amount of U.S. federal net operating losses generated in taxable periods beginning after December 31, 2017 that we are permitted to deduct in any taxable year is limited to 80% of our taxable income in such year, where taxable income is determined without regard to the NOL deduction itself. The Tax Act generally eliminates the ability to carry back any post-2017 NOL to prior taxable years, while allowing unused post-2017 NOLs to be carried forward indefinitely. There is a risk that due to ownership changes, changes in

law or other unforeseen reasons, our existing NOLs could expire or otherwise be unavailable to offset future income tax liabilities.

We do not intend to pay dividends for the foreseeable future and our stock may not appreciate in value.

We currently intend to retain our future earnings, if any, to finance the operation and growth of our business and do not expect to pay any cash dividends in the foreseeable future. As a result, the success of an investment in shares of our common stock will depend upon any future appreciation in its value. There is no guarantee that shares of our common stock will appreciate in value or that the price at which our stockholders have purchased their shares will be able to be maintained.

The requirements of being a public company add to our operating costs and might strain our resources and distract our management.

As a public company, we face increased legal, accounting, administrative and other costs and expenses not faced by private companies. We are subject to the reporting requirements of the Exchange Act, which requires that we file annual, quarterly and current reports with respect to our business and financial condition, and the rules and regulations implemented by the SEC, the Sarbanes-Oxley Act, and the listing standards of the Nasdaq Global Select Market, each of which imposes additional reporting and other obligations on public companies. Although we are currently unable to estimate these costs with any degree of certainty, we expect that the requirements of these rules and regulations will continue to increase our legal, accounting and financial compliance costs, make some activities more difficult, time consuming and costly and place significant strain on our personnel, systems and resources. These increased costs will require us to divert a significant amount of money that we could otherwise use to develop our product candidates or otherwise expand our business. Complying with these requirements might divert management's attention from other business concerns, which could have a material adverse effect on our prospects, business, and financial condition. If we are unable to satisfy our obligations as a public company, we could be subject to delisting of our common stock, fines, sanctions and other regulatory action and potentially civil litigation.

Several provisions of the Delaware General Corporation Law and our charter documents could discourage, delay or prevent a merger or acquisition, which could adversely affect the market price of our securities.

Several provisions of the Delaware General Corporation Law and our charter documents could discourage, delay or prevent a merger or acquisition that stockholders may consider favorable, and the market price of our securities could be reduced as a result. These provisions may include:

- authorizing the issuance of "blank check" preferred stock, the terms of which we may establish and shares of which we may issue without stockholders' approval;
- prohibiting us from engaging in a "business combination" with an "interested stockholder" for a period of three years after the date of the transaction in which the person became an interested stockholder unless certain provisions are met;
- prohibiting cumulative voting in the election of directors;
- prohibiting shareholder action by written consent;
- limiting the persons who may call special meetings of stockholders; and
- establishing advance notice requirements for nominations for election to our board of directors or for proposing matters that can be acted on by stockholders at stockholder meetings.

If securities analysts downgrade our stock or cease coverage of us, the price of our stock could decline.

The trading market for our common stock relies in part on the research and reports that industry or financial analysts publish about us or our business. Currently, a limited number of financial analysts publish reports about us and our business. We do not control these analysts or any other analysts. Furthermore, there are many large, well-established, publicly traded companies active in our industry and market, which may mean that it is less likely that we will receive widespread analyst coverage. If any analyst who covers us downgrades our stock, our stock price could decline rapidly. If one or more analysts cease coverage of our company, we could lose visibility in the market, which in turn could cause our stock price to decline.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

We lease office space for corporate and administrative functions and laboratory space in South San Francisco, California under a sub-sublease that expires in December 2023. The leased location in South San Francisco supports both the HBV Cure and Microbiome programs. Prior to moving into the South San Francisco office and laboratory space in February 2019, we leased office and laboratory space in San Francisco, California under a sublease that expired on February 28, 2019. The leased location in San Francisco, California supported both the HBV Cure and Microbiome programs. We also conduct research, development and small-scale manufacturing activities for the Microbiome program at office and laboratory space in Groton, Connecticut under a lease that expires in March 2021. We also lease office space for administrative functions in Carmel, Indiana under a lease agreement that expires in August 2023. The leased location in Carmel, Indiana provides administrative functions for both the HBV Cure and Microbiome programs.

We believe these leased facilities are adequate for our current needs and that additional space will be available in the future on commercially reasonable terms as needed.

Item 3. Legal Proceedings

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

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 for Common Stock

Our common stock is traded under the symbol "ASMB" and is quoted on the Nasdaq Global Select Market.

Holders of Record

As of February 24, 2020, there were 80 stockholders of record, which excludes stockholders whose shares were held in nominee or street name by brokers.

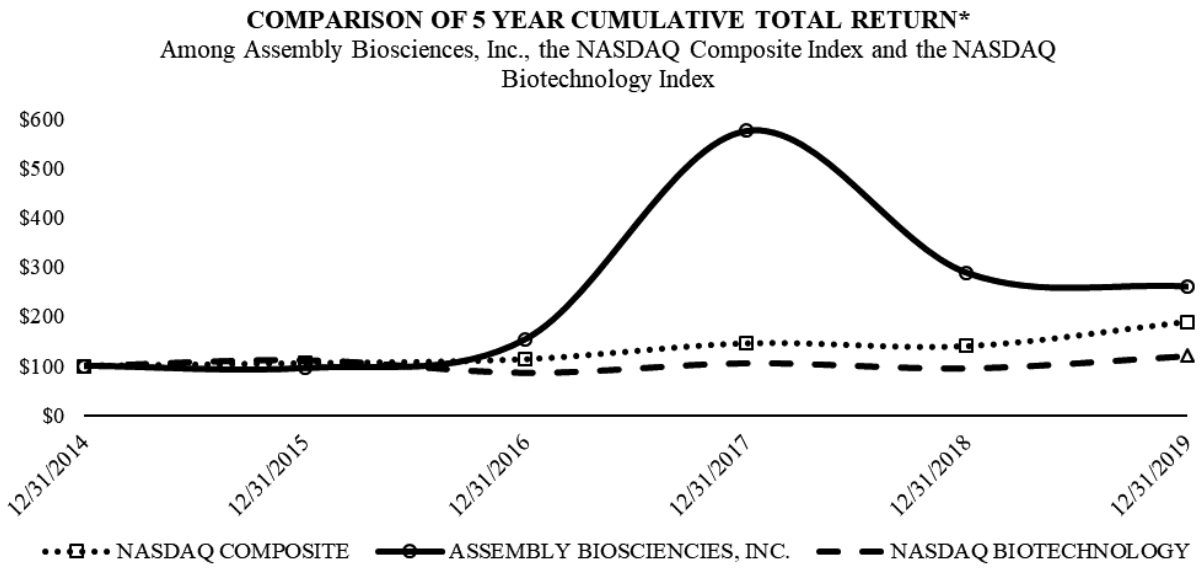
Dividend Policy

We have never declared or paid any dividends and do not anticipate paying any dividends on our common stock in the foreseeable future.

Comparative Stock Performance Graph

The information included under the heading "Comparative Stock Performance Graph" in this Item 5 of Part II of this Form 10-K shall not be deemed to be "soliciting material" or subject to Regulation 14A or 14C, shall not be deemed "filed" for purposes of Section 18 of the Exchange Act, or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act or the Exchange Act.

Set forth below is a graph comparing the total cumulative returns of our common stock, the Nasdaq Composite Index and the Nasdaq Biotechnology Index. The graph assumes $100 was invested in our common stock and each of the indices on December 31, 2014 and that all dividends, if any, are reinvested.



* $100 invested on December 31, 2014 in stock or index, including reinvestment of dividends.

	12/31/2014	12/31/2015	12/31/2016	12/31/2017	12/31/2018	12/31/2019
Assembly Biosciences, Inc.	100.00	95.55	154.58	575.70	287.79	260.31
Nasdaq Composite	100.00	105.73	113.66	145.76	140.10	189.45
Nasdaq Biotechnology	100.00	111.42	87.26	105.64	95.79	119.17

Securities Authorized for Issuance Under Equity Compensation Plans

The following table sets forth the indicated information as of December 31, 2019 with respect to our equity compensation plans.

Plan Category	Number of securities to be issued upon exercise of outstanding options, warrants and rights (a)		Weighted average exercise price of outstanding options, warrants and rights(1) (b)	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a)) (c)	
Equity compensation plans approved by securityholders	5,087,018	(2)	$ 14.93	1,741,525	(3)
Equity compensation plans not approved by securityholders	1,300,349	(4)	$ 19.40	10,425	(5)
Total	6,387,367			1,751,950	

(1) The weighted average exercise price is calculated solely based on the exercise prices of the outstanding stock options and does not reflect the shares that will be issued upon the vesting of outstanding awards of restricted stock units (RSUs), which have no exercise price.

(2) This number includes the following: 469,400 shares subject to stock options granted under the 2010 Equity Incentive Plan (2010 Plan); 2,432,233 shares subject to outstanding awards granted under the Assembly Biosciences, Inc. Amended and Restated 2014 Stock Incentive Plan (2014 Plan), of which 2,199,713 were subject to outstanding stock options and 232,520 were subject to outstanding RSUs; 1,753,947 shares subject to outstanding awards granted under the Assembly Biosciences, Inc. 2018 Stock Incentive Plan, as amended (2018 Plan), of which 1,207,949 were subject to outstanding stock options, 511,198 were subject to outstanding RSUs and 34,800 are underlying stock appreciation rights (which are not included in column (a) but are reflected in column (c)); and 466,238 options assumed by us in connection with our merger with Assembly Pharmaceuticals. This number excludes purchase rights currently accruing under the Assembly Biosciences, Inc. 2018 Employee Stock Purchase Plan (2018 ESPP).

(3) This number includes: no shares under the 2010 Plan, which has been frozen; 217,779 shares available for issuance under the 2014 Plan; 1,204,599 shares available for issuance under the 2018 Plan and; 319,147 shares reserved for issuance under the 2018 ESPP. As of March 2, 2020, assuming each participant purchases the maximum number of shares in the current offering period, no more than 61,000 shares are subject to purchase in the current offering, which ends on May 14, 2020.

(4) This number includes 785,053 shares subject to outstanding awards granted under the 2017 Inducement Award Plan (2017 Inducement Plan), of which 770,053 were subject to outstanding stock options and 15,000 were subject to outstanding RSUs; 500,000 shares subject to stock options granted under the 2019 Inducement Award Plan (2019 Inducement Plan); 15,296 shares subject to warrants granted to one consultant.

(5) This number includes: 10,425 shares available for issuance under the 2017 Inducement Plan and no shares under the 2019 Inducement Plan.

Our stockholder-approved equity compensation plans consist of the 2018 Plan, 2014 Plan, the 2010 Plan, stock options assumed in our merger with Assembly Pharmaceuticals and the 2018 ESPP. Effective on June 2, 2016, the 2010 Plan was frozen, and no further grants will be made under the 2010 Plan. Shares that are forfeited under the 2010 Plan on or after June 2, 2016 will become available for issuance under the 2014 Plan. An "Award" under the 2018 Plan, 2014 Plan or 2010 Plan is any right to receive our common stock consisting of non-statutory stock options, incentive stock options, stock appreciation rights, RSUs, or any other stock award.

In May 2018, our stockholders approved the 2018 ESPP. The 2018 ESPP provides for the purchase by employees of up to an aggregate of 400,000 shares of the Company's common stock. Eligible employees can purchase shares of our common stock at the end of a predetermined offering period at 85% of the lower of the fair market value at the beginning or end of the offering period.

Our outstanding equity compensation arrangements that have not been approved by our stockholders consist of the 2017 Inducement Plan, the 2019 Inducement Plan and warrants to purchase shares of our common stock issued to one consultant. In April 2017, our board of directors adopted the 2017 Inducement Plan and reserved 800,000 shares of our common stock for issuance under the Inducement Plan, and in August 2019, our board of directors adopted the 2019 Inducement Plan and reserved 500,000 shares of our common stock for issuance under the 2019 Inducement Award Plan. The only persons eligible to receive grants of awards under the either the 2017 Inducement Plan or the 2019 Inducement Plan are individuals who satisfy the standards for inducement grants under Nasdaq Marketplace Rule 5635(c)(4) and the related guidance under Nasdaq IM 5635-1-that is, generally, a person not previously an employee or director of ours, or following a bona fide period of non-employment, as an inducement material to the individual's entering into employment with us. An "Award" is any right to receive our common stock pursuant to the Inducement Plan, consisting of nonstatutory stock options, stock appreciation rights, restricted stock awards, RSUs, or any other stock award.

Shelf Registrations

On December 30, 2015, we filed a registration statement on Form S-3 with the SEC using a "shelf" registration process, file number 333-208806, which became effective January 19, 2016 (2016 Registration Statement). Under this shelf registration process, we may from time to time sell any combination of the securities described in the 2016 Registration Statement in one or more offerings for an aggregate offering price of up to $150.0 million. The amount to be registered under the shelf registration consisted of up to $150.0 million of an indeterminate amount of common stock, preferred stock, debt securities, warrants and/or units. There was also registered under the shelf registration an indeterminate number of (i) shares of common stock or other securities of ours as may be issued upon conversion of, or in exchange for, convertible or exchangeable debt securities and/or preferred stock registered under the registration statement, or (ii) shares of preferred stock, common stock, debt securities or units as may be issued upon exercise of warrants registered by the 2016 Registration Statement, as the case may be.

On December 29, 2017, we filed a registration statement on Form S-3 with the SEC using a "shelf" registration process, file number 333-222366, which became effective January 10, 2018 (2018 Registration Statement). Under this shelf registration process, we could from time to time sell any combination of the securities described in the registration statement in one or more offerings for an aggregate offering price of up to $250.0 million. The amount to be registered under the shelf registration consists of up to $250.0 million of an indeterminate amount of common stock, preferred stock, debt securities, warrants and/or units. There is also being registered under the shelf registration a currently indeterminate number of (i) shares of common stock or other securities of ours as may be issued upon conversion of, or in exchange for, convertible or exchangeable debt securities and/or preferred stock registered under the registration statement, or (ii) shares of preferred stock, common stock, debt securities or units as may be issued upon exercise of warrants registered by the 2018 Registration Statement, as the case may be. In connection with the filing of the 2018 Registration Statement, we entered into a sales agreement under which we may offer and sell shares of our common stock having an aggregate offering price of up to $75.0 million under this registration statement through "at the market offerings."

On November 6, 2017, we closed an offering of common stock with an aggregate offering price of approximately $69.3 million under the 2016 Registration Statement. On July 13, 2018, we closed an offering of common stock with an aggregate offering price of $165.6 million under both the 2016 Registration Statement and the 2018 Registration Statement. On December 16, 2019, we closed an offering of a combination of common stock and pre-funded warrants with an aggregate offering price of approximately $143.7 million under the 2018 Registration Statement. As a result of these offerings, no securities remain available under the 2016 Registration Statement and securities

with an aggregate offering price of approximately $21.4 million remain available under the 2018 Registration Statement.

Recent Sales of Unregistered Securities

There were no unregistered sales of equity securities in 2019.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

We did not purchase any of our registered equity securities during the period covered by this Annual Report on Form 10-K.

Item 6. Selected Financial Data

The following selected balance sheet data for the years ended December 31, 2019 and 2018 and the statement of operations data for the years ended December 31, 2019, 2018 and 2017 should be read in conjunction with Part II, Item 7 "Management's Discussion and Analysis of Financial Condition and Results of Operations" and in conjunction with the consolidated financial statements, related notes and other financial information included elsewhere in this Annual Report. The selected consolidated results of operation data for the years ended December 31, 2016 and 2015 and the balance sheet data for the years ended December 31, 2017, 2016 and 2015 have been derived from audited consolidated financial statements not included herein. Our historical results are not necessarily indicative of the results to be expected in the future.

	December 31,				
($ in thousands except for per share amounts)	**2019**	**2018**	**2017**	**2016**	**2015**
Balance Sheet Data:					
Total assets	$ 339,907	$ 268,045	$ 169,303	$ 98,119	$ 133,744
Total stockholders' equity	273,217	210,653	113,120	79,878	118,742
Statement of Operations Data:					
Collaboration revenue	$ 15,963	$ 14,804	$ 9,019	$ —	$ —
Operating expenses	118,676	107,539	61,246	45,278	29,656
Loss from operations	(102,713)	(92,735)	(52,227)	(45,278)	(29,656)
Interest income	4,300	3,083	983	1,539	1,229
Realized gain (loss) from marketable securities	5	—	(615)	(1,140)	(27)
Loss before income taxes	(98,408)	(89,652)	(51,859)	(44,879)	(28,454)
Income tax (expenses) benefit	774	(1,099)	9,050	618	—
Net loss	$ (97,634)	$ (90,751)	$ (42,809)	$ (44,261)	$ (28,454)
Unrealized gain/loss on marketable securities, net of tax	146	45	209	221	(822)
Loss per Shares Data:					
Basic and dilutive loss per share data	$ (3.72)	$ (3.98)	$ (2.41)	$ (2.57)	$ (1.81)

The decrease in total assets from approximately $133.7 million as of December 31, 2015 to approximately $98.1 million as of December 31, 2016 is primarily due to cash used in operations. The increase in total assets from approximately $98.1 million as of December 31, 2016 to approximately $169.3 million as of December 31, 2017 was primarily due to a capital raise of $64.8 million in net proceeds in November 2017 and receipt from Allergan of an upfront payment of $50.0 million in February 2017. The increase in total assets from approximately $169.3 million as of December 31, 2017 to approximately $268.0 million as of December 31, 2018 was primarily due to a capital raise of approximately $155.4 million in net proceeds to us in July 2018. The increase in total assets from approximately $268.0 million as of December 31, 2018 to approximately $339.9 million as of December 31, 2019 is primarily due to a capital raise of $134.7 million in net proceeds in December 2019. Since 2014, our operating expenses have increased primarily due to increases in research and development activities and an increase in our

total headcount from 21 to 115 employees. See, Part II, Item 7 “Management’s Discussion and Analysis of Financial Condition and Results of Operations” for a discussion on results of operations and financing activities since 2017.

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

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with "Selected Financial Data", our consolidated financial statements and the related notes thereto and other financial information appearing elsewhere in this Annual Report on Form 10-K. The following discussion contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those expressed or implied in any forward-looking statements as a result of various factors, including those set forth in this Form 10-K under "Item 1A. Risk Factors."

Overview

We are a clinical-stage biotechnology company advancing two innovative programs: a novel class of oral therapeutic candidates for the treatment of chronic hepatitis B virus (HBV) infection and a novel class of oral live microbial biotherapeutic candidates, which are designed to treat disorders associated with the microbiome.

HBV Cure Program

Over 250 million people worldwide are chronically infected with HBV. Our HBV Cure program is pursuing multiple drug candidates designed to inhibit the HBV lifecycle and block the generation of covalently closed circular DNA (cccDNA), with the aim of increasing the current low cure rate for patients with HBV. We have discovered several novel core inhibitors, which are small molecules that directly target and allosterically modulate the HBV core (HBc) protein.

2019 Developments

ABI-H0731: In November 2019, at the American Association for the Study of Liver Diseases Annual Meeting (The Liver Meeting®), we presented final 24-week data from HBV e antigen (HBeAg) positive patients in our Phase 2 studies of ABI-H0731 (731), our lead HBV core inhibitor product candidate—ABI-H0731-201 (Study 201 in nucleos(t)ide reverse transcriptase inhibitor (NrtI) suppressed patients) and ABI-H0731-202 (Study 202 NrtI-naïve patients). In addition, we presented interim data from an ongoing open-label extension study ABI-H0731-211 (Study 211), where all patients received a combination of 731 and NrtI therapy.

In this analysis, of the 97 patients completing Study 201 or Study 202, 87 were currently receiving a combination of 731 and NrtI therapy and had been treated for at least 16 weeks in Study 211 (cumulative duration of treatment with 731 and NrtI therapy of 16 to more than 40 weeks). 731 was well-tolerated when administered in combination with NrtI therapy with no patients discontinuing treatment due to adverse events (AEs).

As previously reported in the literature, the vast majority of long-term NrtI treated HBeAg positive patients continue to have low level infectious virus, which was confirmed in Study 201 patients at the time of their enrollment. Final Week 24 results from the HBeAg-positive patients (n=47) demonstrated that, among those with detectable HBV DNA at baseline, 22 out of 27 (81%) of patients treated with 731 and NrtI therapy achieved target not detected (TND) by Week 24 compared to zero out of 12 (0%) patients treated with NrtI therapy only ($p<0.001$), as measured with a highly sensitive PCR assay (lower limit of quantification (LLOQ) 5 = IU/mL). These results indicate that the addition of 731 to ongoing NrtI therapy reduced viral burden to levels not achieved by NrtI therapy alone.

Final Week 24 results from treatment-naïve HBeAg-positive patients in Study 202 (n=25) demonstrated faster and deeper HBV DNA declines in patients receiving 731 and entecavir (ETV) than those receiving ETV alone. Statistically significant reductions of viral pre-genomic RNA (pgRNA) were observed by Week 2 with 731 and ETV ($p<0.001$).

Longer-term treatment with 731 and NrtI therapy resulted in deeper reductions in HBV DNA and pgRNA. In the analysis, 21 out of 25 patients from Study 202 who were in treatment in Study 211 demonstrated mean HBV DNA and pgRNA declines from baseline of 6.3 logs and 3.0 logs, respectively, at Week 48. Of the 27 NrtI-suppressed HBeAg-positive patients who had received 731 and NrtI therapy for at least 40 weeks in Study 201 and were on treatment in Study 211, 18 (67%) achieved HBV DNA TND + pgRNA less than 35 U/mL, along with significant declines in HBeAg and HBcrAg levels in some of these patients.

An important finding based on interim data from Study 211 is the observed correlation between pgRNA and viral antigens. Eleven out of 21 (52%) patients from Study 202 that are now on Study 211 who have been treated with 731 and NrtI therapy for 16 to 60 weeks have achieved decreases in pgRNA of greater than 3 logs. The results in the table below demonstrate that these larger declines in pgRNA were associated with observed reductions in viral antigens. As cccDNA is the only known source of pgRNA, significant declines in pgRNA, coupled with multi-log declines in viral antigens in some patients, suggests that cccDNA pool levels may be decreasing.

Number	<40 U/L	Log_{10} Decrease	Mean Log Reductions at Last Time Point (range)			Patients Exhibiting ≥0.5 Log Decline (%)		
Patients	ALT	pgRNA	HBeAg	HBcrAg	HBsAg	HBeAg	HBcrAg	HBsAg
11	10	>3.0	1.03 (0.0-2.5)	1.42 (0.0-3.1)	0.86 (0.0-3.6)	9 (82)	10 (91)	6 (55)
8	8	2.0-3.0	0.34 (0.1-0.7)	0.45 (0.1-1.0)	0.14 (0.0-0.5)	2 (25)	6 (75)	1 (13)
2	2	<2.0	0.15 (0.9-1.8)	0.29 (0.3-0.3)	0.17 (0.0-0.3)	0 (0)	0 (0)	0 (0)

From the final summary of safety findings in Study 201 and Study 202, 731 when administered with a NrtI therapy for 24 weeks was well-tolerated in both HBeAg-positive and -negative patients with no AEs leading to discontinuation, no Grade 3 or 4 AEs and no serious AEs reported. Five patients receiving 731 and NrtI reported a rash (four Grade 1 and one Grade 2). No associated systemic signs or laboratory abnormalities were observed, and all patients continued treatment through Week 24. Overall, laboratory abnormalities observed were of Grade 1 or 2 severity and occurred in similar proportions of patients across the two treatment groups. With longer-term ongoing treatment in Study 211, interim data indicated that the nature, frequency and severity of AEs and laboratory abnormalities observed were similar to those observed during the initial 24-week treatment period. Study 211 is ongoing, and we expect to continue to report interim, as well as final, data from this study.

ABI-H2158: We presented final data from the Phase 1a portion of the Phase 1a/1b dose-ranging clinical study of ABI-H2158 (2158) at the Annual Meeting of the European Association for the Study of the Liver (EASL) in April 2019. The Phase 1a study assessed safety, tolerability and pharmacokinetics (PK) in 48 healthy volunteers. 2158 was well tolerated following single and multiple ascending doses. There were no dose dependent treatment-emergent AEs and no pattern of clinical safety or laboratory abnormalities observed within or across any cohorts. Once daily administration is projected to result in trough liver concentrations in excess of the in vitro EC50 of 334 nM at which cccDNA establishment is inhibited by 50%. We initiated the Phase 1b dose-ranging portion of this study in April 2019 to assess the safety, PK and antiviral activity of 2158 in patients with chronic HBV infection.

In November 2019, at The Liver Meeting®, we reported interim data from the first, low-dose cohort of the Phase 1b portion of the Phase 1a/1b dose-ranging clinical study, which is currently enrolling HBeAg-positive patients in sequential dose cohorts of nine patients, with each cohort randomized to receive oral 2158 or placebo (7:2) once daily for 14 days. The interim data from the initial cohort receiving the lowest dose of 2158 at 100 mg demonstrated potent antiviral activity at this initial dose level, reflected by mean declines from baseline to day 15 of 2.3 log_{10} [range 1.7 – 3.0] and 2.1 log_{10} [range 1.5 – 2.7] in HBV DNA and pgRNA, respectively.

No serious AEs, dose limiting toxicities or premature discontinuations have been reported to date. All AEs were Grade 1. One patient assigned to placebo and three patients on 2158 reported AEs that resolved without intervention: dizziness, fatigue, rash, headache and upper abdominal pain. Observed steady-state exposures were in excess of the EC90 for in vitro antiviral and cccDNA assays. We believe that the safety and PK data and parameters from this interim analysis support once daily administration and the continued evaluation of 2158 across the planned dose cohorts in patients with chronic HBV infection. Following completion of the Phase 1b dose-ranging study, we expect to initiate a Phase 2 clinical study in the second quarter of 2020.

Microbiome Program

In recent years, there has been increasing scientific evidence suggesting the therapeutic potential of the human microbiome—the billions of microbes living in and on people-to impact health and disease. Our Microbiome program builds upon experience reported in the literature of successfully treating various disease indications with fecal microbiota transplants (FMT) and seeks to provide a pharmacologically relevant therapy using a “drug like” approach that delivers targeted and specific microbiome therapies in an oral capsule.

Our Microbiome program consists of a fully integrated platform that includes a strain isolation, identification, characterization and function based selection process, methods for strain purification and growth under conditions compliant with Good Manufacturing Practice (cGMP) requirements, and a licensed patented delivery system that we call GEMICEL®, which is designed to allow for targeted oral delivery of live biologic and conventional therapies to the lower gastrointestinal (GI) tract.

2019 Developments

In February 2019, we initiated a Phase 1b human clinical study of ABI-M201 (M201) to evaluate the safety of M201 and its effects on disease activity measures in patients with mildly to moderately active ulcerative colitis (UC) and ongoing treatment with mesalamine. The study's primary objective is safety and tolerability, and its secondary objectives focus on the effect of M201 treatment in patients with UC.

The study will consist of two sequential, non-overlapping cohorts of patients, separated by intervening interim analysis. Both cohorts will involve eight weeks of study drug treatment. Interim data from the initial treatment cohort (Cohort A), consisting of 20 patents, will inform the decision to advance to the second cohort (Cohort B), consisting of 24 patients, and its dose selection. The patients in Cohort A will be randomized 1:1 to receive either one daily capsule of M201 or placebo in addition to their treatment with mesalamine. The patients in Cohort B will be randomized 3:1 to receive between one to five daily capsules of M201 or placebo in addition to their treatment with mesalamine. In June 2019, we initiated dosing of the first patient in this clinical study.

Collaboration Agreement

On January 6, 2017, we entered into the Research, Development, Collaboration and License Agreement (the Collaboration Agreement) with Allergan to develop and commercialize select microbiome gastrointestinal programs. Pursuant to the terms of the Collaboration Agreement, Allergan paid us an upfront payment of $50.0 million in February 2017. Additionally, we are eligible to receive up to approximately $631.0 million in payments related to seven development milestones and up to approximately $2.14 billion in payments related to 12 commercial development and sales milestones in connection with the successful development and commercialization of licensed compounds for up to six different indications. We have agreed with Allergan to share development costs up to an aggregate of $75.0 million through proof-of-concept (POC) studies on a ⅓, ⅔ basis, respectively, and Allergan has agreed to assume all post-POC development costs. Additionally, we have an option to co-promote the licensed programs in the United States and China, subject to certain conditions set forth in the Collaboration Agreement.

Operations

We currently have corporate and administrative offices and research laboratory space in South San Francisco, California and research, development and small-scale manufacturing activities in Groton, Connecticut and administrative offices in Carmel, Indiana.

Since our inception, we have had no revenue from product sales and have funded our operations principally through debt financings prior to our initial public offering in 2010 and through equity financings and collaborations since then. Our operations to date have been primarily limited to organizing and staffing our company, licensing our product candidates, discovering and developing our product candidates, establishing small-scale manufacturing capabilities for certain of our product candidates, maintaining and improving our patent portfolio and raising capital. We have generated significant losses to date, and we expect to continue to generate losses as we continue to develop our product candidates. As of December 31, 2019, we had an accumulated deficit of approximately $439.4 million. Because we do not generate revenue from any of our product candidates, our losses will continue as we further develop and seek regulatory approval for, and commercialize, our product candidates. As a result, our operating losses are likely to be substantial over the next several years as we continue the development of our product candidates and thereafter if none are approved or successfully launched. We are unable to predict the extent of any future losses or when we will become profitable, if at all.

Financial Operations Overview

Research and Development Expense

Research and development expenses consist primarily of costs incurred for our research activities, including our drug discovery efforts, target validation, lead optimization and the development of our product candidates, which include:

- employee-related expenses including salaries, benefits, and stock-based compensation expense;
- expenses incurred under agreements with third parties, including contract research organizations (CROs) that conduct research and development, nonclinical and clinical activities on our behalf and the cost of

consultants, and contract manufacturing organizations (CMOs) that manufacture all of our drug substance and the drug product used in our HBV-cure program;

- the cost of lab supplies and acquiring, developing, and manufacturing nonclinical and, in the case of our Microbiome program, early stage clinical study materials;

- fees related to our license agreements; and

- facilities, depreciation, and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance, and other operating costs.

Research and development costs are expensed as incurred. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are rendered.

We use our employee and infrastructure resources across multiple research and development programs, and we allocate internal employee-related and infrastructure costs, as well as certain third-party costs, to each of our programs based on the personnel resources allocated to such program. Our research and development expenses, by major program, are outlined in the table below (in thousands):

	Year Ended December 31,		
	2019	2018	2017
HBV	$ 50,843	$ 41,486	$ 23,221
Microbiome[(1)]	23,538	19,435	15,581
Stock- based compensation	11,376	11,820	5,423
Total	$ 85,757	$ 72,741	$ 44,225

(1) Expenses presented for Microbiome do not reflect reimbursement of expenses under the Collaboration Agreement with Allergan as discussed in Note 8 to the Consolidated Financial Statements.

The successful discovery and development of our product candidates is highly uncertain. As such, at this time, we cannot reasonably estimate, or know the nature, timing and estimated costs, of the efforts that will be necessary to complete the remainder of their development. We are also unable to predict when, if ever, material net cash inflows will commence from our product candidates. This is due to the numerous risks and uncertainties associated with developing medicines, including the uncertainty of:

- the timing, progress and success of our Phase 2 clinical development of 731, our Phase 1 and potential Phase 2 clinical development of 2158, our Phase 1 clinical development of M201, and our nonclinical and planned clinical development activities for 3733 and other product candidates we may identify in each of the HBV Cure and Microbiome programs;

- establishing an appropriate safety profile with IND-enabling toxicology studies sufficient to advance additional product candidates into clinical development;

- successful enrollment in, and completion of, clinical studies;

- receipt of marketing approvals from applicable regulatory authorities;
- establishing internal commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;
- launching commercial sales of the products, if and when approved, whether alone or in collaboration with others; and
- maintaining a continued acceptable safety profile of the products following approval and wide use.

A change in the outcome of any of these variables or variables discussed in "Item 1A. Risk Factors" with respect to the development of any of our product candidates would significantly change the costs and timing associated with the development of that product candidate.

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical studies. We expect research and development costs to increase significantly for the foreseeable future as our product candidate development programs progress. However, we do not believe that it is possible at this time to accurately project total program-specific expenses through commercialization. There are numerous factors associated with the successful commercialization of any of our product candidates, including future trial design and various regulatory requirements, many of which cannot be determined with accuracy at this time based on our stage of development. Additionally, future commercial and regulatory factors beyond our control will impact our clinical development programs and plans.

General and administrative expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in executive, finance, accounting, business development, legal and human resources functions. Other significant costs include facility costs not otherwise included in research and development expenses, insurance costs, legal fees relating to patents and corporate matters and fees for accounting and consulting services.

We anticipate that our general and administrative expenses will increase in the future to support continued research and development activities, potential commercialization of our product candidates and increased costs of operating as a public company. These increases will likely include increased costs related to the hiring of additional personnel and fees to outside consultants, lawyers and accountants, among other expenses. Additionally, we anticipate increased costs associated with being a public company, including expenses related to services associated with maintaining compliance with exchange listing and U.S. Securities and Exchange Commission (SEC) requirements, insurance, and investor relations costs.

Interest income

Interest income consists of interest earned on our cash and cash equivalents and available-for-sale securities.

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 consolidated financial statements, which we have 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 assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported amounts of revenues and expenses during the reporting periods. We evaluate our estimates and judgments, including those described in greater detail below, on an ongoing basis. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

While our significant accounting policies are described in more detail in the notes to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K, we believe that the following accounting

policies are the most critical to aid you in fully understanding and evaluating our financial condition and results of operations.

Revenue Recognition

At the inception of an arrangement, we evaluate if a counterparty to a contract is a customer, if the arrangement is within the scope of revenue from contracts with customers guidance, and the term of the contract. We recognize revenue when the customer obtains control of promised goods or services in a contract for an amount that reflects the consideration we expect to receive in exchange for those goods or services. For contracts with customers, we apply the following five-step model in order to determine this amount: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations, including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) we satisfy each performance obligation. Our performance obligations under these arrangements may include licenses of intellectual property, options to license additional intellectual property, research and development services, delivery of manufactured product, and/or participation on joint steering committees. Allergan can select backups and additional target indications to add to the licenses granted and also has the ability to enter into a contract manufacturing agreement with us for compound supply, and we have concluded that these rights are options. We evaluated whether such options contained material rights and concluded they were not offered at a discount that exceeds discounts available to other customers, and therefore were not material rights. The grant of additional licensing rights upon option exercises and contract manufacturing agreements will be accounted for as separate contracts when they occur.

We provide standard indemnification and protection of licensed intellectual property for our customer. These provisions are part of assurance that the licenses meet the agreement's, representations and are not obligations to provide goods or services.

We only apply the five-step model to contracts when it is probable that we will collect the consideration to which we are entitled in exchange for the goods or services we transfer to the customer. As part of the accounting for contracts with customers, we must develop assumptions that require judgment to determine the standalone selling price of each performance obligation identified in the contract. We then allocate the total transaction price to each performance obligation based on the estimated standalone selling prices of each performance obligation. We estimated standalone selling prices of our performance obligations using income-based valuation approach for the estimated value a licensor of the compounds would receive. We recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when the performance obligation is satisfied or as it is satisfied. We recognize revenues for each of our distinct performance obligations as the related research and development services are performed because our customer consumes the benefit of research and development work simultaneously as we perform these services.

Upfront License Fees

If a license to our intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, we recognize revenues from nonrefundable, upfront license fees based on the relative value prescribed to the license compared to the total value of the arrangement. The revenue is recognized when the license is transferred to the collaborator and the collaborator is able to use and benefit from the license. For licenses that are not distinct from other obligations identified in the arrangement, we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time. If the combined performance obligation is satisfied over time, we apply an appropriate method of measuring progress for purposes of recognizing revenue from nonrefundable, upfront license fees. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

Development and Regulatory Milestone Payments

Depending on facts and circumstances, we may record revenues from certain milestones in a reporting period before the milestone is achieved if we conclude that achievement of the milestone is probable and that recognition of revenue related to the milestone will not result in a significant reversal in amounts recognized in future periods. We record a corresponding contract asset when this conclusion is reached. Milestone payments that have not been included in the transaction price to date are fully constrained. We re-evaluate the probability of achievement of such milestones and any related constraint each reporting period. We adjust our estimate of the overall transaction price, including the amount of collaborative revenue that was recorded, if necessary.

Research and Development Service Payments

We are reimbursed at a certain percentage for performing research and development services based on hours worked by our employees at a fixed contractual rate per hour and third-party pass-through costs we incur on a quarterly basis. Research and development service payments are included in the transaction price in the reporting period that we conclude that it is probable that recording revenue in the period will not result in a significant reversal in amounts recognized in future periods. Accounts receivable are recorded when the right to the research and development service payment consideration becomes unconditional. We record the full reimbursed portion of these expenses as collaboration revenue in our consolidated statements of operations as we consider performing research and development services to be a part of our ongoing and central operations.

Sales-based Milestone and Royalty Payments

Our customer may be required to pay us sales-based milestone payments or royalties on future sales of commercial products. We recognize revenues related to sales-based milestone and royalty payments upon the later to occur of (i) achievement of the collaborator's underlying sales or (ii) satisfaction of any performance obligation(s) related to these sales, in each case assuming our licensed intellectual property is deemed to be the predominant item to which the sales-based milestones and/or royalties relate.

We receive payments from our customer based on billing schedules established in each contract. Upfront payments and fees are recorded as deferred revenue upon receipt or when due until we perform our obligations under the arrangement. If the related performance obligation is expected to be satisfied within the next 12 months, these amounts will be classified in current liabilities. We recognize a contract asset relating to our conditional right to consideration that is not subject to a constraint. Amounts are recorded as accounts receivable when our right to consideration is unconditional. A net contract asset or liability is presented for each contract with a customer. We do not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the customer and the transfer of the promised goods or services to the customer will be one year or less.

We may be required to exercise considerable judgment in estimating revenue to be recognized. Judgment is required in identifying performance obligations, estimating the transaction price, estimating the standalone selling prices of identified performance obligations, which may include forecasted revenue, development timelines, reimbursement rates for personnel and other research and development costs, discount rates and probabilities of technical and regulatory success, and estimating the progress towards satisfaction of performance obligations.

On January 1, 2018, we adopted ASU No. 2014-09, *Revenue from Contracts with Customers*, as amended (Accounting Standards Codification Topic 606) (ASC 606) using the modified retrospective method applied to those contracts which were not completed as of January 1, 2018. We also elected to use the practical expedient that allows an entity to expense the incremental cost of obtaining a contract as an expense when incurred if the amortization period of the asset that an entity otherwise would have recognized is less than one year. Results for the year ended December 31, 2018 are presented under ASC 606, while prior period amounts are not adjusted and continue to be reported in accordance with historic accounting under previous revenue recognition guidance. As of the adoption date of ASC 606, we had only one contract with a customer, Allergan, that had not been completed. Based on our analysis, we concluded there was no significant change in applying ASC 606 to our agreement with Allergan and no amounts have been recognized within "accumulated deficit" in the consolidated balance sheet related to the adoption of the new standard.

Goodwill and Indefinite-Lived Intangible Assets

Goodwill and indefinite-lived intangible assets are reviewed for impairment at least annually in the fourth quarter and more frequently if events or other changes in circumstances indicate that the carrying amount of the assets may not be recoverable. Impairment of goodwill and indefinite-lived intangibles is determined to exist when the fair value is less than the carrying value of the net assets being tested.

Goodwill

We determined that we have only one operating segment and reporting unit. Accordingly, our review of goodwill impairment indicators is performed at the entity-wide level. In performing each annual impairment assessment and any interim impairment assessment, we determine if we should qualitatively assess whether it is more likely than not that the fair value of goodwill is less than its carrying amount (the qualitative impairment test). Some of the factors considered in the assessment include general macroeconomic conditions, conditions specific to the industry and market, cost factors, the overall financial performance and whether there have been sustained declines in our share price. If we conclude it is more likely than not that the fair value of the reporting unit is less than its carrying amount, or elect not to use the qualitative impairment test, a quantitative impairment test is performed using a two-step process. The first step of the goodwill qualitative impairment assessment compares the fair value of the reporting unit to its carrying value. If the fair value of the reporting unit exceeds its carrying amount, goodwill of the reporting unit is considered not impaired, and the second step of the impairment test is not required. We use our market capitalization as an indicator of fair value. We believe that since our reporting unit is publicly traded, the ability of a controlling shareholder to benefit from synergies and other intangible assets that arise from control might cause the fair value of our reporting unit as a whole to exceed our market capitalization. However, we believe that the fair value measurement need not be based solely on the quoted market price of an individual share of our common stock, but also can consider the impact of a control premium in measuring the fair value of its reporting unit. Should our market capitalization be less than our total stockholders' equity as of our annual test date or as of any interim impairment testing date, we would also consider market comparables, recent trends in our stock price over a reasonable period and, if appropriate, use an income approach (discounted cash flow) to determine whether the fair value of our reporting unit is greater than our carrying amount. If we were to use an income approach, we would establish a fair value by estimating the present value of our projected future cash flows expected to be generated from our business. The discount rate applied to the projected future cash flows to arrive at the present value would be intended to reflect all risks of ownership and the associated risks of realizing the stream of projected future cash flows. Our discounted cash flow methodology would consider projections of financial performance for a period of several years combined with an estimated residual value. The most significant assumptions we would use in a discounted cash flow methodology are the discount rate, the residual value and expected future revenues, gross margins and operating costs, along with considering any implied control premium. The second step, if required, compares the implied fair value of the reporting unit goodwill with the carrying amount of that goodwill. If the carrying amount of the reporting unit's goodwill exceeds its implied fair value, an impairment charge is recognized in an amount equal to that excess. Implied fair value is the excess of the fair value of the reporting unit over the fair value of all identified assets and liabilities. In 2019, we elected to bypass the qualitative goodwill impairment assessment. As of October 1, 2019, we have determined through a quantitative impairment test that the fair value significantly exceeded the carrying value of our single reporting unit, and concluded that goodwill was not impaired. We did not recognize any goodwill impairment in any of the years presented.

Indefinite-Lived Intangible Asset

Our indefinite-lived intangible asset consists of in-process research and development (IPR&D) projects acquired in a business combination that are used in research and development activities but have not yet reached technological feasibility, regardless of whether they have alternative future use. The primary basis for determining the technological feasibility or completion of these projects is obtaining regulatory approval to market the underlying products in an applicable geographic region. We classify in-process research and development acquired in a business combination as an indefinite-lived intangible asset until the completion or abandonment of the associated research and development efforts. Upon completion of the associated research and development efforts, we perform a final test for impairment and will determine the useful life of the technology and begin amortizing the assets to reflect their use over their remaining lives. Upon permanent abandonment, we would write off the remaining carrying amount of the associated IPR&D intangible asset.

In performing each annual impairment assessment and any interim impairment assessment, we determine if we should qualitatively assess whether it is more likely than not that the fair value of our IPR&D asset is less than its carrying amount (the qualitative impairment test). If we conclude that is the case, or elect not to use qualitative impairment test, we would proceed with quantitatively determining the fair value of the IPR&D asset and comparing its fair value to its carrying value to determine the amount of impairment, if any (the quantitative impairment test).

In performing the qualitative impairment test, we consider the results of the most recent quantitative impairment test and identifies the most relevant divers of the fair value for the IPR&D asset. The most relevant drivers of fair value we have identified are consistent with the assumptions used in the quantitative estimate of the IPR&D asset discussed below. Using these drivers, we identify events and circumstances that may have an effect on the fair value of the IPR&D asset since the last time the IPR&D's fair value was quantitatively determined. We then weigh these factors to determine and conclude if it is not more likely than not that the IPR&D asset is impaired. If it is more likely than not that the IPR&D asset is impaired we proceed with quantitatively determining the fair value of the IPR&D asset.

We use the income approach to determine the fair value of our IPR&D asset. This approach calculates fair value by estimating the after-tax cash flows attributable to an in-process project over its useful life and then discounting these after-tax cash flows back to a present value. This estimate includes significant assumptions regarding the estimates that market participants would make in evaluating the IPR&D asset, including the probability of successfully completing clinical trials and obtaining regulatory approval to market the IPR&D asset, the timing of and the expected costs to complete IPR&D projects, future net cash flows from potential drug sales, which are based on estimates of the sales price of the drug, the number of patients who will be diagnosed and treated and our competitive position in the marketplace, and appropriate discount and tax rates. Any impairment to be recorded is calculated as the difference between the fair value of the IPR&D asset as of the date of the assessment with the carrying value of the IPR&D asset on our consolidated balance sheet.

For 2019, we elected to perform a qualitative impairment test and concluded that it is more likely than not that the fair value of our IPR&D asset exceeded the carrying value and no further testing was required. We did not recognize any IPR&D impairment in any of the years presented.

For asset purchases outside of business combinations, we expense any purchased research and development assets as of the acquisition date if they have no alternative future uses.

Research and Development Expense and Accruals

Research and development costs include personnel-related costs, outside contracted services including clinical study costs, facilities costs, fees paid to consultants, milestone payments prior to FDA approval, license fees prior to FDA approval, professional services, travel costs, dues and subscriptions, depreciation and materials used in clinical trials and research and development and costs incurred under the Collaboration Agreement. Research and development costs are expensed as incurred unless there is an alternative future use in other research and development projects. Payments made prior to the receipt of goods or services to be used in research and development are capitalized until the goods or services are received. Such payments are evaluated for current or long-term classification based on when they will be realized or consumed. Assets acquired as part of an asset acquisition that are used in research and development or are IPR&D are immediately expensed as research and development unless there is an alternative future use in other research and development projects.

As part of the process of preparing our consolidated financial statements, we are required to estimate certain research and development expenses. This process involves reviewing quotations and contracts, reviewing the terms of our license agreements, communicating with our vendors and applicable 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. Payments made prior to the receipt of goods or services to be used in research and development are capitalized until the goods or services are received. Such payments are evaluated for current or long-term classification based on when they will be realized or consumed. Examples of estimated amortized or accrued research and development expenses include fees to:

- CROs and other service providers in connection with clinical studies;
- CMOs in connection with the production of clinical trial materials; and
- vendors in connection with preclinical development activities.

We base our expenses related to clinical studies on our estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and contract research organizations that conduct and manage clinical studies 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 and expense recognition. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In either amortizing or accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the related prepayment or accrual accordingly. Our understanding of the status and timing of services performed relative to the actual status and timing of services performed may vary and may result in our reporting changes in estimates in any particular period. Adjustments to prior period estimates have not been material for the years ended December 31, 2019 and 2018.

Stock-Based Compensation

For equity awards that vest subject to the satisfaction of service requirements, compensation expense is measured based on the fair value of the award on the date of grant and is recognized as expense on a straight-line basis over the requisite service period. Stock-based awards with graded vesting schedules are recognized using the accelerated attribution method on a straight-line basis over the requisite service period for each separately vesting portion of the award. For stock awards which have a performance condition, compensation cost is measured based on the fair value on the grant date (the date performance targets are established) and is expensed over the requisite service period for each separately vesting tranche when achievement of the performance objective becomes probable. We assess the probability of the performance conditions being met on a continuous basis. Forfeitures are recognized when incurred.

The fair value of restricted stock units (RSUs) is determined based on the number of shares granted and the quoted market price of our common stock on the date of grant. The fair value of stock options is estimated on the date of grant using the Black-Scholes option pricing model (Black-Scholes Model). The fair value of stock-based payment awards as determined by the Black-Scholes Model are affected by our stock price as well as other assumptions. These assumptions include, but are not limited to, the expected term, the expected stock price volatility, the risk-free interest rate and the expected dividend yield. We have, due to insufficient historical data, used the "simplified method" to determine the expected term of stock options granted with a service condition. If any of the assumptions used in the Black-Scholes Model change significantly, stock-based compensation expense may differ materially in the future from that recorded in the current period.

We account for stock-based compensation arrangements with non-employees, which primarily consist of consultants, using a fair value approach. The fair value of these options is measured using the Black-Scholes Model reflecting the same assumptions as applied to employee options in each of the reported periods, other than the expected life, which is assumed to be the remaining contractual life of the option. The compensation costs of these arrangements are subject to remeasurement over the vesting terms as earned.

We expect to continue to grant stock options and other equity awards in the future, and to the extent that we do, our actual stock-based compensation expense recognized in future periods will likely increase.

Off-Balance Sheet Arrangements

Since our inception, we have not engaged in any off-balance sheet arrangements, including the use of structured finance, special purpose entities or variable interest entities.

Contractual Obligations

We have contractual and commercial obligations under our operating lease commitments and licenses. The following table summarizes our future contractual obligations and commercial commitments at December 31, 2019 (in thousands):

	Payments Due By Period				
	Less than 1 year	1-3 years	3-5 years	More than 5 years	Total
Operating lease obligations	$ 4,583	$ 7,229	$ 3,303	$ —	$ 15,115
License obligations	175	75	—	—	250
Total contractual obligations	$ 4,758	$ 7,304	$ 3,303	$ —	$ 15,365

In general, milestone and royalty payments associated with certain license agreements have not been included in the above table of contractual obligations, because we cannot reasonably estimate if or when they will occur. The milestone payments included in the table of contractual obligations above are payments we believe are reasonably likely to occur during the indicated time periods. Excluded from the table are future research and development expenses under the Collaboration Agreement of up to $25.0 million. We enter into contracts in the normal course of business with CROs for clinical trials and CMO's for clinical supply manufacturing and with vendors for preclinical research studies and other services and products for operating purposes, which generally provide for termination within 30 days of notice, and therefore, are cancelable contracts and not included in the table above. Further, we anticipate that our operating lease obligations will be higher than projected as we renew existing real estate leases that expire in 2020 and enter into new or expanded real estate leases.

Results of Operations

General

At December 31, 2019, we had an accumulated deficit of approximately $439.4 million primarily as a result of research and development expenses and general and administrative expenses. While we may in the future generate revenue from a variety of sources, including license fees, milestone payments, research and development payments in connection with strategic partnerships and/or product sales, our product candidates are at an early stage of development and may never be successfully developed or commercialized. Accordingly, we expect to continue to incur substantial losses from operations for the foreseeable future and there can be no assurance that we will ever generate significant revenues.

Comparison of the Years Ended December 31, 2019 and 2018

Collaboration Revenue

During the year ended December 31, 2019, we generated approximately $16.0 million of collaboration revenue, which included the amortization of deferred revenue and reimbursement revenue in each case incurred under the Collaboration Agreement, an increase of approximately $1.2 million from approximately $14.8 million for the same period in 2018. The increase was based on increased research efforts performed during 2019 for our Microbiome program.

Research and Development Expense

Research and development expense, excluding stock-based compensation expense, was approximately $74.4 million for the year ended December 31, 2019, an increase of approximately $13.5 million from approximately $60.9 million for the same period in 2018. The increase in research and development expenses was primarily due to an increase of approximately $9.4 million in research expenses for our HBV-cure program and an increase of approximately $4.1 million in research expenses for our Microbiome program.

Stock-based compensation expense was approximately $11.4 million for the year ended December 31, 2019, a decrease of approximately $0.4 million from approximately $11.8 million for the year ended December 31, 2018.

General and Administrative Expense

General and administrative expense, excluding stock-based compensation expense, was approximately $23.7 million for the year ended December 31, 2019, an increase of approximately $5.6 million from approximately $18.1 million for the same period in 2018. The increase in general and administrative expenses was primarily due to an increase of approximately $3.5 million in employee related expenses due to the addition of employees in executive management, finance and human resources. This increase also includes a one-time expense of $1.7 million for severance packages in conjunction with the relocation of our corporate headquarters to South San Francisco, California effective January 1, 2020, the departure of one of our former executives, $0.9 million in rent expenses for our new office in South San Francisco and $0.3 million in professional expenses.

Stock-based compensation expense was approximately $9.2 million for the year ended December 31, 2019, a decrease of approximately $7.5 million from approximately $16.7 million for the year ended December 31, 2018. The decrease was primarily due to a $4.3 million one-time expense related to the departure and transition to consultant of one of our former executive officers in 2018 coupled with the reversal of previously recognized expense of $3.6 million related to forfeited awards resulting from the departure of one of our former executive officers in 2019.

Interest and Other Income

Interest and other income was approximately $4.3 million for the year ended December 31, 2019 compared to approximately $3.1 million for the same period in 2018. Interest income for the years ended December 31, 2019 and 2018 was primarily related to interest income earned on marketable securities, corporate bonds and money market funds as a result of higher balances carried in 2019.

Income Tax (Expense) Benefit

Income tax benefit for the year ended December 31, 2019 was approximately $0.8 million compared to an income tax expense for year ended December 31, 2018 of $1.1 million. The income tax benefit in the current year is primarily due to a change in the Company's state and local effective tax rate and recording the impact of certain indefinite-lived deferred tax asset carryforwards. The income tax expense recognized in the prior year is primarily due to a change in our state and local effective tax rate.

Comparison of the Years Ended December 31, 2018 and 2017

Research and Development Expense

Research and development expense, excluding stock-based compensation expense, was approximately $60.9 million for the year ended December 31, 2018, an increase of approximately $22.1 million from approximately $38.8 million for the same period in 2017. The increase in research and development expenses was primarily due to an increase of approximately $18.3 million in research expenses for our HBV-cure program and an increase of approximately $3.9 million for nonclinical development of our Microbiome program.

Stock-based compensation expense was approximately $11.8 million for the year ended December 31, 2018, an increase of approximately $6.4 million from approximately $5.4 million for the year ended December 31, 2017.

General and Administrative Expense

General and administrative expense, excluding stock-based compensation expense, was approximately $18.1 million for the year ended December 31, 2018, an increase of approximately $4.3 million from approximately $13.8 million for the same period in 2017. The increase in general and administrative expenses was primarily due to an increase of approximately $2.1 million in salary and benefits expenses due to additional employees in information technology, human resources and finance, $0.6 million in office and equipment rent expenses, $0.4 million in professional expenses, $0.4 million in recruitment expenses, $0.3 million in tax expenses, $0.2 million in insurance expenses and $0.2 million in legal expenses.

Stock-based compensation expense was approximately $16.7 million for the year ended December 31, 2018, an increase of approximately $13.5 million from approximately $3.2 million for the year ended December 31, 2017. The increase was due, in part, to a $4.3 million one-time expense related to the departure and transition to consultant of one of our former executive officers and an incremental expense of approximately $5.0 million was recognized due to the addition of a new executive officer in 2017.

Interest and Other Income

Interest and other income was approximately $3.1 million for the year ended December 31, 2018 compared to approximately $1.0 million for the same period in 2017. Interest income for the years ended December 31, 2018 and 2017 was primarily related to interest income on marketable securities, corporate bonds and money market funds.

Income Tax (Expense) Benefit

Income tax expense for the year ended December 31, 2018 was approximately $1.1 million compared to an income tax benefit for year ended December 31, 2017 of $9.1 million. The income tax expense in the current year is primarily due to a change in the Company's realizability of its state and local effective tax rate. The income tax benefit recognized in the prior year is primarily due to the Tax Cuts and Jobs Act of 2017 (the Tax Act) enacted on December 22, 2017, which reduced the U.S. federal corporate tax rate to 21%. The changes effected by the Tax Act resulted in tax benefit of $9.1 million, of which $8.6 million relates to the Tax Act.

Liquidity and Capital Resources

As a result of our significant research and development expenditures and the lack of any FDA-approved products to generate product sales revenue, we have not been profitable and have generated operating losses since we were incorporated in October 2005. We have funded our operations through December 31, 2019 principally with debt prior to our initial public offering, and thereafter with equity financing, raising an aggregate of approximately $546.4 million in net proceeds from public offerings and private placements from inception to December 31, 2019. Additionally, in February 2017, we received a $50.0 million upfront payment in connection with the execution of the Collaboration Agreement.

In November 2017, we sold to various investors an aggregate of 2,541,000 shares of common stock in a public offering at $27.25 per share, which included the exercise in full by the underwriters of their option to purchase 331,500 additional shares of common stock. We received aggregate net proceeds of approximately $64.8 million from the offering and option exercise, after deducting underwriting discounts and commissions and offering expenses.

In July 2018, we sold to various investors an aggregate of 4,600,000 shares of common stock in a public offering at $36.00 per share, which included the exercise in full by the underwriters of their option to purchase 600,000 additional shares of common stock. We received aggregate net proceeds of approximately $155.4 million from the offering and the option exercise, after deducting underwriting discounts and commissions and offering expenses payable.

In December 2019, we sold to various investors an aggregate of 6,287,878 shares of common stock at a public offering price of $16.50 per share, which included the exercise in full by the underwriters of their option to purchase 1,136,363 shares of common stock, and pre-funded warrants to purchase 2,424,242 shares of common stock at a public offering price of $16.499. We received aggregate net proceeds of approximately $134.7 million from the offering and the option exercise, after deducting underwriting discounts and commissions and offering expenses payable.

Cash Flows

A summary of our cash flows for the periods presented was as follows:

	Year Ended December 31,		
	2019	**2018**	**2017**
Operating activities	$ (84,067)	$ (64,958)	$ 1,860
Investing activities	(50,318)	(135,397)	(15,642)
Financing activities	139,646	159,793	67,240
Net increase (decrease) in cash and cash equivalents	$ 5,261	$ (40,562)	$ 53,458

Net Cash (Used in) Provided by Operating Activities

Net cash used in operating activities was approximately $84.1 million for the year ended December 31, 2019. This was primarily due to approximately $97.6 million of net loss, a decrease of $9.5 million of operating assets and liabilities, approximately $0.8 million of deferred income tax benefit and $1.7 million of amortization of discount on marketable securities, which were offset by a $20.6 million non-cash expense recorded for stock-based compensation, $4.5 million of amortization of operating lease right-of-use assets and approximately $0.5 million of depreciation and amortization expense.

Net cash used in operating activities was approximately $65.0 million for the year ended December 31, 2018. This was primarily due to approximately $90.8 million of net loss, a decrease of $4.2 million of operating assets and liabilities and $0.2 million of amortization of discount on marketable securities, which were offset by a $28.5 million non-cash expense recorded for stock-based compensation, $0.6 million of depreciation and amortization expense and approximately $1.1 million of deferred income tax expenses.

Net cash provided by operating activities was approximately $1.9 million for the year ended December 31, 2017 and funded our research and development program build out and general and administrative expenses. Net cash provided by continuing operations for the year ended December 31, 2017 was primarily driven by approximately $8.6 million non-cash expenses recorded for the stock-based compensation, an approximately $44.3 million increase in cash from changes in operating assets and liabilities (primarily due to an increase in deferred revenue of $45.8 million related to the Collaboration Agreement) and $0.6 million realized loss from marketable securities, and offset by an approximately $42.8 million net loss and $9.1 million deferred income tax benefit.

Net Cash Used in Investing Activities

Net cash used in investing activities for the year ended December 31, 2019 was approximately $50.3 million primarily due to a purchase of approximately $281.3 million marketable securities and $1.6 million of fixed assets, which were offset by approximately $203.9 million for the redemption of marketable securities and $28.7 million for the sale of marketable securities.

Net cash used in investing activities for the year ended December 31, 2018 was approximately $135.4 million primarily due to a purchase of approximately $183.9 million marketable securities and $0.3 million of fixed assets and construction in progress, which were offset by approximately $48.9 million for the redemption of marketable securities.

Net cash used in investing activities for the year ended December 31, 2017 was approximately $15.6 million primarily due to the purchase of approximately $48.2 million of marketable securities and $0.9 million of fixed assets, and offset by a $33.5 million redemption of marketable securities during the year.

Net Cash Provided by Financing Activities

Net cash provided by financing activities for the year ended December 31, 2019 was approximately $139.6 million resulting from the net proceeds of approximately $134.7 million from our public offering of 6,287,878 shares of common stock and 2,424,242 pre-funded warrants to purchase 2,424,242 shares of common stock at a public offering price of $16.499, including 1,136,363 shares of common stock purchased by the underwriters pursuant to their 30-day option to purchase additional shares, approximately $4.2 million from the exercise of stock options to purchase 585,292 shares of common stock and approximately $0.7 million from the issuance of 59,370 shares of common stock under our 2018 ESPP .

Net cash provided by financing activities for the year ended December 31, 2018 was approximately $159.8 million, resulting from the net proceeds of approximately $155.4 million from our public offering of 4,600,000 shares of common stock, including 600,000 shares of common stock purchased by the underwriters pursuant to their 30-day option to purchase additional shares, and approximately $4.0 million from the exercise of stock options to purchase 775,224 shares of common stock.

Net cash provided by financing activities in the year ended December 31, 2017 was approximately $67.2 million, resulting from the net proceeds of approximately $64.8 million from our public offering of 2,541,500 shares of common stock, including 331,500 shares of common stock purchased by the underwriters pursuant to their 30-day option to purchase additional shares, and approximately $2.4 million from the exercise of stock options to purchase 353,612 shares of common stock resulting in 349,720 shares issued due to utilization of net exercise provisions by some option holders.

Future Funding Requirements

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the research, development and clinical studies of our product candidates and pursue our intellectual property strategy. Furthermore, we expect to continue to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts.

We monitor our cash needs and the status of the capital markets on a continuous basis. From time to time, we opportunistically raise capital and have done so numerous times since our initial public offering by issuing equity securities, most recently in December 2019. We expect to continue to raise capital when and as needed and at the time and in the manner most advantageous to us.

We expect that our existing cash, cash equivalents and marketable securities, will enable us to fund our operating expenses and capital expenditure requirements for at least the next twelve months. Our future capital requirements will depend on many factors, including:

- the scope, progress, results and costs of our ongoing drug discovery, nonclinical development, laboratory testing and clinical studies of our product candidates and any additional clinical studies we may conduct in the future;
- the extent to which we further acquire or in-license other product candidates and technologies;
- our ability to manufacture, and to contract with third parties to manufacture, adequate supplies of our product candidates for our clinical studies and any eventual commercialization;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs of preparing, filing and prosecuting patent applications in the United States and abroad, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims; and
- our ability to establish and maintain collaborations on favorable terms, if at all.

Identifying potential product candidates and conducting nonclinical testing and clinical studies is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of medicines that we do not expect to be commercially available for many years, if at all. Accordingly, we will need to continue to rely on additional financings to achieve our business objectives. Adequate additional financings may not be available to us on acceptable terms, or at all.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise funds through additional collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Recent Accounting Pronouncements

See Note 2 of notes to the consolidated financial statements for a discussion of recent accounting standards and pronouncements.

Cautionary Statement

We operate in a highly competitive environment that involves a number of risks, some of which are beyond our control. The following statement highlights some of these risks. For more detail, see "Item 1A. Risk Factors."

Statements contained in this Form 10-K that are not historical facts, are or might constitute forward-looking statements under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Although we believe the expectations reflected in such forward-looking statements are based on reasonable assumptions, our expectations might not be attained. Forward-looking statements involve known and unknown risks that could cause actual results to differ materially from expected results. Factors that could cause actual results to differ materially from our expectations expressed in the report include, among others: risks related to the costs, timing, regulatory review and results of our nonclinical studies and clinical studies; our ability to obtain FDA approval of our product candidates; our anticipated capital expenditures, our estimates regarding our capital requirements, and our need for future capital; our liquidity and working capital requirements; our expectations regarding our revenues, expenses and other results of operations; the unpredictability of the size of the markets for, and market acceptance of, any of our products; our ability to sell any approved products and the price we are able realize; our ability to establish and maintain collaborations on favorable terms; our ability to obtain future funding on acceptable terms; our ability to hire and retain necessary employees and to staff our operations appropriately; our ability to compete in our industry and innovation by our competitors; our ability to stay abreast of and comply with new or modified laws and regulations that currently apply or become applicable to our business; estimates and estimate methodologies used in preparing our financial statements; the future trading prices of our common stock and the impact of securities analysts' reports on these prices; and the risks set out in our filings with the SEC.

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.

We do not believe that our cash and equivalents have significant risk of default or illiquidity. Under our current investment policies, we invest our cash and cash equivalents in money market funds which invest in short-term U.S. Treasury securities with insignificant rates of return. We also invest our cash and cash equivalents in readily marketable, high-quality securities that are diversified and structured to minimize market risks. Our exposure to market risk for changes in interest rates relates primarily to our investments in marketable securities. Marketable securities held in our investment portfolio are subject to changes in market value in response to changes in interest rates and liquidity. A significant change in market interest rates could have a material impact on interest income earned from our investment portfolio. Changes in interest rates may affect the fair value of our investment portfolio; however, we will not recognize such gains or losses in our statement of operations and comprehensive income (loss) unless the investments are sold.

While we believe our cash and equivalents 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 equivalents at one or more financial institutions that are in excess of federally insured limits.

Inflation generally affects us by increasing our cost of labor and clinical study costs. We do not believe that inflation has had a material effect on our results of operations during 2019, 2018 or 2017.

Item 8. Financial Statements and Supplementary Data

The financial statements required to be filed pursuant to this Item 8 are appended to this report. An index of those financial statements is found on page F-1.

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 maintain a system of disclosure controls and procedures, as defined in Rule 13a-15(e) promulgated under the Securities and Exchange Act of 1934, as amended (the Exchange Act), that is designed to provide reasonable assurance that information, which is required to be disclosed in our reports filed pursuant to the Exchange Act, is accumulated and communicated to management in a timely manner. At the end of fiscal year ending December 31, 2019, we carried out an evaluation, under the supervision, and with the participation of, our management, including our Chief Executive Officer and our Chief Financial Officer, of the effectiveness of the design and operation of our disclosure controls and procedures pursuant to Exchange Act Rule 13a-15(b). Based upon that evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures for the fiscal year ending as of December 31, 2019 were effective at reasonable assurance levels.

Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Exchange Act Rule 13a-15(f). Our internal control over financial reporting is designed to provide reasonable assurance to our management and Board of Directors regarding the preparation and fair presentation of published financial statements. A control system, no matter how well designed and operated, can only provide reasonable, not absolute, assurance that the objectives of the control system are met. Because of these inherent limitations, management does not expect that our internal controls over financial reporting will prevent all error and all fraud. Under the supervision and with the participation of our management, including our Chief Executive Officer and our Chief Financial Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based on the framework in Internal Control-Integrated Framework issued in 2013 by the Committee of Sponsoring Organizations of the Treadway Commission. Based on our evaluation under the

framework in Internal Control-Integrated Framework, our management concluded that our internal control over financial reporting was effective as of December 31, 2019.

Our independent registered public accounting firm, Ernst & Young LLP has issued an opinion on the effectiveness of our internal control over financial reporting as of December 31, 2019. The report of Ernst & Young LLP is included with the financial statements appended to this Form 10-K pursuant to Item 8.

Changes in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting in the fourth quarter of 2019 that materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

Not applicable.

PART III

ITEM 10. Directors, Executive Officers and Corporate Governance

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

Code of Ethics

Our Board has adopted a Code of Ethics for our principal executive officer and all senior financial officers and a Code of Conduct applicable to all of our employees and our directors. Both Codes are available under the "Investors—Corporate Governance" section of our website at www.assemblybio.com. If we make any substantive amendments to, or grant any waivers from, the Code of Ethics for our principal executive officer, principal financial officer, principal accounting officer, controller or persons performing similar functions, or any officer or director, we will disclose the nature of such amendment or waiver on our website or in a Current Report on Form 8-K.

Section 16(a) Beneficial Ownership Reporting Compliance

Pursuant to Section 16(a) of the Securities Exchange Act, our directors and executive officers are required to file reports with the SEC indicating their holdings of and transactions in our equity securities. To our knowledge, based solely on our review of the copies of such reports furnished to us and written representations that our officers, directors and holders of more than 10% of our common stock complied with all applicable filing requirements during the fiscal year ended December 31, 2019.

ITEM 11. Executive Compensation

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

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

Except for the table regarding equity compensation plans, which is included in Part II Item 5 of this Annual Report on Form 10-K, the information required by this item will be contained in the Proxy Statement and is incorporated into this Annual Report on Form 10-K by reference.

ITEM 13. Certain Relationships and Related Party Transactions, and Director Independence

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

ITEM 14. Principal Accounting Fees and Services

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

ITEM 15. Exhibits, Financial Statement Schedules

(a) *Exhibits.* The following exhibits are filed as part of this registration statement:

Exhibit Number	Description of Document	Registrant's Form	Dated	Exhibit No.	Filed Herewith
3.1	Fourth Amended and Restated Certificate of Incorporation dated May 31, 2018.	8-K	06/01/2018	3.1	
3.2	Amended and Restated Bylaws as amended through August 6, 2019.	10-Q	11/7/2019	3.1	
4.1	Specimen of Common Stock Certificate.	S-3	12/30/2015	4.1	
4.2	Form of Pre-Funded Warrant.	8-K	12/16/2019	4.1	
4.3	Description of Securities				X
10.1	Sub-Sublease, dated as of July 18, 2018, between Prothena Biosciences, Inc., as Sub-Sublandlord, and Assembly Biosciences, Inc., as Sub-Subtenant.	10-Q	11/08/2018	10.1	
10.2*	Exclusive License Agreement dated September 3, 2013 by and between The Indiana University Research and Technology Corporation and Assembly Pharmaceuticals, Inc.	10-Q	11/17/2014	10.29	
10.3*	License and Collaboration Agreement dated November 8, 2013, by and between Ventrus Biosciences, Inc. and Therabiome, LLC.	10-K	03/31/2014	10.22	
10.4*	Research, Development, Collaboration and License Agreement dated January 6, 2017 between Assembly Biosciences, Inc. and Allergan Pharmaceuticals International Limited.	10-Q	05/8/2017	10.1	
10.5#	Employment Agreement, dated August 6, 2019, between Assembly Biosciences, Inc. and John G. McHutchison, A.O., M.D.	10-Q	11/07/2019	10.1	
10.6#	Employment Agreement, dated September 30, 2019, between Assembly Biosciences, Inc. and Thomas J. Russo, effective as of October 28, 2019.	10-Q	11/07/2019	10.6	
10.7#	Employment Agreement, dated October 22, 2019, between Assembly Biosciences, Inc. and Luisa M. Stamm, M.D., Ph.D. effective as of November 6, 2019.				X
10.8#	Employment Agreement, dated December 17, 2015, between Assembly Biosciences, Inc. and Richard Colonno, Ph.D., effective as of January 5, 2016.	10-Q	11/9/2016	10.1	
10.9#	Amendment No. 1 to Employment Agreement, dated October 10, 2018, between Assembly Biosciences, Inc. and Richard Colonno, Ph.D.	8-K	10/12/2018	10.2	
10.10#	Amended and Restated Employment Agreement, dated October 10, 2018, between Assembly Biosciences, Inc. and Jackie Papkoff, Ph.D.	10-K	02/28/2019	10.11	
10.11#	2010 Equity Incentive Plan	S-1/A	10/4/2010	10.14	
10.12#	Assembly Biosciences, Inc. Amended and Restated 2014 Stock Incentive Plan.	8-K	6/6/2016	10.1	
10.13#	Form of Notice of Stock Option Grant and Stock Option Agreement under Amended and Restated 2014 Stock Incentive Plan.	S-8	9/17/2014	10.28	
10.14#	Form of Restricted Stock Unit Award Notice and Restricted Stock Unit Award Agreement under the Amended and Restated 2014 Stock Incentive Plan.	10-Q	11/01/2017	10.1	
10.15#	Assembly Biosciences, Inc. 2017 Inducement Award Plan (the 2017 Inducement Award Plan).	10-Q	08/09/2017	10.1	
10.16#	Form of Notice of Stock Option Grant and Stock Option Agreement under the 2017 Inducement Award Plan.	10-Q	08/09/2017	10.2	
10.17#	Form of Restricted Stock Unit Award Notice and Restricted Stock Unit Award Agreement under the 2017 Inducement Award Plan.	10-Q	08/09/2017	10.3	
10.18#	Assembly Biosciences, Inc. 2018 Stock Incentive Plan.	8-K	6/1/2018	10.1	
10.19#	Amendment No. 1 to Assembly Biosciences, Inc. 2018 Stock Incentive Plan	8-K	05/21/2019	10.2	

Exhibit Number	Description of Document	Registrant's Form	Dated	Exhibit No.	Filed Herewith
10.20#	Form of Notice of Stock Option Grant and Stock Option Agreement under the 2018 Stock Incentive Plan.	8-K	6/1/2018	10.2	
10.21#	Form of Restricted Stock Unit Award Notice and Restricted Stock Unit Award Agreement under the 2018 Stock Incentive Plan.	8-K	6/1/2018	10.3	
10.22#	Form of Stock Appreciation Right Award Agreement for Non-U.S. Grantees under the Assembly Biosciences, Inc. 2018 Stock Incentive Plan.	8-K	10/12/2018	10.4	
10.23#	Assembly Biosciences, Inc. 2018 Employee Stock Purchase Plan.	8-K	6/1/2018	10.4	
10.24#	Assembly Biosciences, Inc. 2019 Inducement Award Plan	10-Q	11/07/2019	10.4	
10.25#	Form of Notice of Stock Option Grant and Stock Option Agreement under the 2019 Inducement Award Plan.	10-Q	11/07/2019	10.5	
10.26#†	Separation Agreement, dated August 6, 2019, between Assembly Biosciences, Inc. and Derek A. Small.	10-Q	11/07/2019	10.2	
10.27#†	Consulting Agreement, effective January 1, 2020, between Assembly Biosciences, Inc. and Derek A. Small.	10-Q	11/07/2019	10.3	
10.28#†	Separation Agreement, dated May 6, 2019, between Assembly Biosciences, Inc. and Uri A. Lopatin, M.D..	10-Q	08/05/2019	10.1	
10.29#†	Consulting Agreement, effective May 7, 2019, between Assembly Biosciences, Inc. and Uri A. Lopatin, M.D..	10-Q	08/05/2019	10.2	
21.1	List of Subsidiaries of Assembly Biosciences, Inc.				X
23.1	Consent of Independent Registered Public Accounting Firm.				X
24.1	Power of Attorney (included on signature page)				X
31.1	Certification of the Chief Executive Officer Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				X
31.2	Certification of the Chief Financial Officer Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.				X
32.1‡	Certification of the Chief Executive Officer Pursuant to 18 U.S.C. Section 1350 as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				X
32.2‡	Certification of the Chief Financial Officer Pursuant to 18 U.S.C. Section 1350 as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				X
101.INS	Inline XBRL Instance Document.				
101.SCH	Inline XBRL Taxonomy Extension Schema Document.				
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document.				
101.DEF	Inline XBRL Taxonomy Extension Definitions 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).				

* Certain information in this exhibit has been omitted and filed separately with the Securities and Exchange Commission pursuant to a confidential treatment request.

\# Represents management contracts or compensatory plans or arrangements.

† Portions of this exhibit (indicated by asterisks) have been omitted in accordance with the rules of the Securities and Exchange Commission.

‡ The certifications attached as Exhibits 32.1 and 32.2 that accompany this Annual Report on Form 10-K are to be deemed furnished and shall not be deemed "filed" with the SEC and are not to be incorporated by reference into any filing of Assembly Biosciences, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Annual Report on Form 10-K, irrespective of any general incorporation language contained in such filing.

Item 16. Form 10-K Summary.

None

SIGNATURES

In accordance with Section 13 or 15(d) of the Securities Exchange Act, the Registrant caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

ASSEMBLY BIOSCIENCES, INC.

Date: March 4, 2020

By: /s/ John G. McHutchison, A.O., M.D.
Name: John G. McHutchison, A.O., M.D.
Title: Chief Executive Officer and President

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints John G. McHutchison, A.O., M.D., Thomas J. Russo, CFA and Elizabeth H. Lacy, jointly and severally, his or her attorneys-in-fact, each with the power of substitution, for him or her in any and all capacities, to sign any amendments to this report, and to file the same, with exhibits thereto and other documents in connection therewith with the Securities and Exchange Commission, hereby ratifying and confirming all that each of said attorneys-in-fact, or his or her substitute or substitutes may 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 by the following persons on behalf of the registrant in the capacities and on the dates indicated.

Signature	Title	Date
/s/ John G. McHutchison, A.O., M.D. John G. McHutchison, A.O., M.D.	Chief Executive Officer, President and Director (Principal Executive Officer)	March 4, 2020
/s/ Thomas J. Russo, CFA Thomas J. Russo, CFA	Chief Financial Officer (Principal Financial and Principal Accounting Officer)	March 4, 2020
/s/ William R. Ringo, Jr. William R. Ringo, Jr.	Chairman of the Board	March 4, 2020
/s/ Anthony E. Altig Anthony E. Altig	Director	March 4, 2020
/s/ Mark Auerbach Mark Auerbach	Director	March 4, 2020
/s/ Richard D. DiMarchi, Ph.D. Richard D. DiMarchi, Ph.D.	Director	March 4, 2020
/s/ Myron Z. Holubiak Myron Z. Holubiak	Director	March 4, 2020
/s/ Helen S. Kim Helen S. Kim	Director	March 4, 2020
/s/Alan J. Lewis, Ph.D. Alan J. Lewis, Ph.D.	Director	March 4, 2020
/s/ Susan Mahony, Ph.D. Susan Mahony, Ph.D.	Director	March 4, 2020
/s/ Derek A. Small Derek A. Small	Director	March 4, 2020

ASSEMBLY BIOSCIENCES, INC.
FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Assembly Biosciences, Inc.

Opinion on the Financial Statements

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

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2019, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 Framework) and our report dated March 4, 2020 expressed an unqualified opinion thereon.

Adoption of New Accounting Standards

As discussed in Note 2 to the consolidated financial statements, the Company changed its method of accounting for leases in 2019 due to the adoption of Accounting Standards Update (ASU) No. 2016-02, Leases (Topic 842), and the related amendments, effective January 1, 2019, using the modified retrospective approach.

As discussed in Note 2 to the consolidated financial statements, the Company changed its method of accounting for revenue in 2018 due to the adoption of Accounting Standards Update (ASU) No. 2014-09, Revenue from Contracts with Customers (Topic 606), and the related amendments, effective January 1, 2018, using the modified retrospective method.

Basis for Opinion

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

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP
We have served as the Company's auditor since 2015.

Redwood City, California
March 4, 2020

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Assembly Biosciences, Inc.

Opinion on Internal Control over Financial Reporting

We have audited Assembly Biosciences, Inc.'s internal control over financial reporting as of December 31, 2019, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, Assembly Biosciences, Inc. (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2019, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2019 and 2018, the related consolidated statements of operations and comprehensive loss, changes in stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2019, and the related notes and our report dated March 4, 2020 expressed an unqualified opinion thereon.

Basis for Opinion

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

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

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

/s/ Ernst & Young LLP

Redwood City, California
March 4, 2020

ASSEMBLY BIOSCIENCES, INC.
CONSOLIDATED BALANCE SHEETS
(In thousands except for share amounts and par value)

	As of December 31,	
	2019	**2018**
ASSETS		
Current assets		
Cash and cash equivalents	$ 46,732	$ 41,471
Marketable securities	227,311	176,609
Accounts receivable from collaboration	3,374	2,430
Prepaid expenses and other current assets	5,363	1,992
Total current assets	282,780	222,502
Property and equipment, net	1,830	557
Operating lease right-of-use assets	11,975	—
Other assets	1,684	3,348
Indefinite-lived intangible asset	29,000	29,000
Goodwill	12,638	12,638
Total assets	**$ 339,907**	**$ 268,045**
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities		
Accounts payable	$ 1,731	$ 3,693
Accrued clinical expenses	4,826	3,561
Other accrued expenses	8,286	6,118
Deferred revenue - short-term	6,411	5,100
Operating lease liabilities - short-term	3,186	—
Total current liabilities	24,440	18,472
Deferred rent	—	108
Deferred tax liabilities	2,531	3,252
Deferred revenue - long-term	30,637	35,560
Operating lease liabilities - long-term	9,082	—
Total liabilities	**66,690**	**57,392**
Commitments and contingencies		
Stockholders' equity		
Preferred stock, $0.001 par value; 5,000,000 shares authorized; no shares issued or outstanding	—	—
Common stock, $0.001 par value; 100,000,000 shares authorized as of December 31, 2019 and 2018; 32,558,307 and 25,495,425 shares issued and outstanding as of December 31, 2019 and 2018, respectively	32	25
Additional paid-in capital	712,807	552,762
Accumulated other comprehensive loss	(201)	(347)
Accumulated deficit	(439,421)	(341,787)
Total stockholders' equity	273,217	210,653
Total liabilities and stockholders' equity	**$ 339,907**	**$ 268,045**

See Accompanying Notes to the Consolidated Financial Statements

ASSEMBLY BIOSCIENCES, INC.
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(In thousands except for share and per share amounts)

	Year ended December 31,		
	2019	**2018**	**2017**
Collaboration revenue	$ 15,963	$ 14,804	$ 9,019
Operating expenses:			
Research and development	85,757	72,741	44,225
General and administrative	32,919	34,798	17,021
Total operating expenses	118,676	107,539	61,246
Loss from operations	**(102,713)**	**(92,735)**	**(52,227)**
Other income (expenses)			
Interest and other income	4,300	3,083	983
Other income (expense), net	5	—	(615)
Total other income	4,305	3,083	368
Loss before income taxes	**(98,408)**	**(89,652)**	**(51,859)**
Income tax benefit (expense)	774	(1,099)	9,050
Net loss	**$ (97,634)**	**$ (90,751)**	**$ (42,809)**
Other comprehensive income			
Unrealized gain on marketable securities, net of tax	146	45	209
Comprehensive loss	**$ (97,488)**	**$ (90,706)**	**$ (42,600)**
Net loss per share, basic and diluted	$ (3.72)	$ (3.98)	$ (2.41)
Weighted average common shares outstanding, basic and diluted	26,258,790	22,801,644	17,750,380

See Accompanying Notes to the Consolidated Financial Statements

ASSEMBLY BIOSCIENCES, INC.
CONSOLIDATED STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY
(In thousands except for share amounts)

	Common Stock		Additional Paid-in	Accumulated Other Comprehensive	Accumulated	Total Stockholders'
	Shares	Amount	Capital	Loss	Deficit	Equity
Balance as of December 31, 2016	**17,246,754**	**$ 17**	**288,689**	**(601)**	**(208,227)**	**79,878**
Sale of common stock, net of underwriters' discount and costs	2,541,500	3	64,845	—	—	64,848
Issuance of common stock upon exercise of stock options	349,720	—	2,393	—	—	2,393
Unrealized gain on marketable securities, net of tax	—	—	—	209	—	209
Stock-based compensation	—	—	8,601	—	—	8,601
Net loss	—	—	—	—	(42,809)	(42,809)
Balance as of December 31, 2017	**20,137,974**	**$ 20**	**364,528**	**(392)**	**(251,036)**	**113,120**
Sale of common stock, net of underwriters' discount and costs	4,600,000	4	155,421	—	—	155,425
Issuance of common stock upon exercise of stock options	735,030	1	3,959	—	—	3,960
Issuance of common stock under Employee Stock Purchase Plan (ESPP)	21,483	—	408	—	—	408
Issuance of shares of common stock for settlement of restricted stock units (RSUs)	938	—	—	—	—	—
Unrealized gain on marketable securities, net of tax	—	—	—	45	—	45
Stock-based compensation	—	—	28,446	—	—	28,446
Net loss	—	—	—	—	(90,751)	(90,751)
Balance as of December 31, 2018	**25,495,425**	**$ 25**	**552,762**	**(347)**	**(341,787)**	**210,653**
Sale of common stock and pre-funded warrants, net of underwriters' discount and costs	6,287,878	6	134,655	—	—	134,661
Issuance of common stock upon exercise of stock options	585,292	1	4,237	—	—	4,238
Settlement of RSUs for cash	—	—	(4)	—	—	(4)
Issuance of common stock under ESPP	59,370	—	747	—	—	747
Issuance of shares of common stock for settlement of RSUs	130,342	—	—	—	—	—
Unrealized gain on marketable securities, net of tax	—	—	—	146	—	146
Stock-based compensation	—	—	20,410	—	—	20,410
Net loss	—	—	—	—	(97,634)	(97,634)
Balance as of December 31, 2019	**32,558,307**	**$ 32**	**712,807**	**(201)**	**(439,421)**	**273,217**

See Accompanying Notes to the Consolidated Financial Statements

ASSEMBLY BIOSCIENCES, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

	Year Ended December 31,		
	2019	**2018**	**2017**
Cash flows from operating activities			
Net loss	$ (97,634)	$ (90,751)	$ (42,809)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	494	643	219
Stock-based compensation	20,558	28,485	8,601
Net accretion and amortization of investments in marketable securities	(1,735)	(229)	—
Non-cash rent expense	4,454	—	—
Deferred income tax (benefit) expense	(774)	1,099	(9,050)
Loss on disposal of fixed assets	102	—	—
Other	(5)	—	615
Changes in operating assets and liabilities:			
Accounts receivable from collaboration	(944)	(156)	(2,273)
Prepaid expenses and other current assets	(3,685)	(1,094)	(286)
Other assets	1,664	(3,008)	(84)
Accounts payable	(1,962)	1,569	(244)
Accrued clinical expenses	1,265	3,119	(242)
Other accrued expenses	2,016	382	1,628
Deferred revenue	(3,612)	(5,125)	45,785
Deferred rent	—	108	—
Operating lease liabilities	(4,269)	—	—
Net cash (used in) provided by operating activities	(84,067)	(64,958)	1,860
Cash flows from investing activities			
Purchases of property and equipment	(1,554)	(340)	(865)
Purchases of marketable securities	(281,334)	(183,941)	(48,234)
Proceeds from maturities of marketable securities	203,911	48,884	33,457
Proceeds from sale of marketable securities	28,659	—	—
Net cash used in investing activities	(50,318)	(135,397)	(15,642)
Cash flows from financing activities			
Proceeds from common stock and pre-funded warrants sold, net of underwriters' discount and costs	134,661	155,425	64,847
Proceeds from the issuance of common stock under ESPP	747	408	—
Proceeds from the exercise of stock options	4,238	3,960	2,393
Net cash provided by financing activities	139,646	159,793	67,240
Net increase (decrease) in cash and cash equivalents	5,261	(40,562)	53,458
Cash and cash equivalents at the beginning of the period	41,471	82,033	28,575
Cash and cash equivalents at the end of the period	**$ 46,732**	**$ 41,471**	**$ 82,033**
Supplemental non-cash investing and financing activities			
Operating lease liabilities arising from obtaining right-of-use assets	$ 15,261	$ -	$ -

See Accompanying Notes to the Consolidated Financial Statements

Note 1 - Nature of Business

Overview

Assembly Biosciences, Inc., together with its subsidiaries (Assembly or the Company), incorporated in Delaware in October 2005, is a clinical-stage biotechnology company advancing two innovative programs: a novel class of oral therapeutic candidates for the treatment of hepatitis B virus (HBV) infection and a novel class of oral live microbial biotherapeutic candidates, which are designed to treat disorders associated with the microbiome. The Company operates in one segment and, as of December 31, 2019, was headquartered in Carmel, Indiana with operations in South San Francisco, California and Groton, Connecticut. Effective January 1, 2020, the Company changed its corporate headquarters to its South San Francisco, California facility. The Company expects to continue maintaining its office in Carmel, Indiana for a period of time.

The Company's HBV-cure program is pursuing multiple drug candidates that inhibit the HBV lifecycle and block the generation of covalently closed circular DNA (cccDNA), with the aim of increasing the current low cure rates for patients with chronic HBV infection. Assembly has discovered multiple novel core inhibitors, which are small molecules that directly target and allosterically modify the HBV core (HBc) protein.

The Company's Microbiome program consists of a fully integrated platform that includes a disease-targeted strain isolation, identification, characterization and selection process, methods for strain purification and growth under current Good Manufacturing Practice (cGMP) conditions, and a licensed patented delivery system that the Company calls GEMICEL®, which is designed to allow for targeted oral delivery of live biologic and conventional therapies to the lower gastrointestinal (GI) tract. Using the Company's microbiome platform capabilities, the Company is exploring product candidates for multiple disease indications, including ulcerative colitis (UC), Crohn's disease and irritable bowel syndrome (IBS) with Allergan Pharmaceuticals International Limited (Allergan) in connection with its Research, Development, Collaboration, and License Agreement (the Collaboration Agreement), as well as immune-mediated and metabolic disorders and oncology, which indications the Company will pursue either internally or in collaboration with other parties.

Liquidity

The Company has not derived any revenue from product sales to date and currently has no approved products. Once a product has been developed, it will need to be approved for sale by the U.S. Food and Drug Administration (FDA) or an applicable foreign regulatory agency. Since inception, the Company's operations have been financed primarily through the sale of equity securities, the proceeds from the exercise of warrants and stock options, the issuance of debt, an upfront payment related to the Collaboration Agreement, and research and development cost reimbursements from the Collaboration Agreement. The Company has incurred losses from operations since inception and expects to continue to incur substantial losses for the next several years as it continues its product development efforts. Management believes the Company currently has sufficient funds to meet its operating requirements for at least the next twelve months following the date that these consolidated financial statements are issued. If the Company cannot generate significant cash from its operations, it intends to obtain any additional funding it requires through strategic relationships, public or private equity or debt financings, grants or other arrangements (see Note 6 for recent sales of common stock). The Company cannot assure such funding will be available on reasonable terms, if at all.

If the Company is unable to generate enough revenue from the Collaboration Agreement when needed or to secure additional sources of funding and receive related full and timely collections of amounts due, it may be necessary to significantly reduce the current rate of spending through reductions in staff and delaying, scaling back, or stopping certain research and development programs, including more costly clinical trials.

Note 2 - Summary of Significant Accounting Policies and Recent Accounting Pronouncements

Basis of Presentation

These consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States (U.S. GAAP) and include the accounts of the Company and its wholly owned subsidiaries. All intercompany balances and transactions have been eliminated in consolidation.

Use of Estimates

The preparation of consolidated financial statements in conformity with the accounting principles generally accepted in the United States of America (U.S. GAAP) requires management to make estimates and assumptions that may affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and reported amounts of expenses during the reporting period. Actual results could differ from those estimates.

Significant estimates inherent in the preparation of the accompanying consolidated financial statements include revenue recognition, clinical trial accruals, recoverability and useful lives (indefinite or finite) of intangible assets, assessment of impairment of goodwill, provisions for income taxes, amounts receivable under the Collaboration Agreement, measurement of operating lease liabilities, and the fair value of stock options, stock appreciation rights, and restricted stock units (RSUs) granted to employees, directors, and consultants.

The Company's estimates could be affected by external conditions, including those unique to the Company and general economic conditions. It is reasonably possible that these external factors could have an effect on the Company's estimates and could cause actual results to differ from those estimates and assumptions.

Cash and cash equivalents

All highly liquid investments with original maturities of three months or less at the time of purchase are considered to be cash equivalents. All of the Company's cash equivalents have liquid markets and high credit ratings. The Company maintains its cash in bank deposits and other accounts, the balances of which, at times and at December 31, 2019 and 2018, exceed federally insured limits.

Investments in Marketable Securities

The Company invests its excess cash in debt securities with high credit ratings including but not limited to money market funds, asset backed securities, securities issued by the U.S. government and its agencies, corporate debt securities and commercial paper. The Company has designated its investments in marketable securities as available-for-sale and measures these securities at their respective fair values. Marketable securities are classified as short-term or long-term based on the maturity date and their availability to meet current operating requirements. Marketable securities that mature in one year or less are classified as short-term available-for-sale securities and are reported as a component of current assets.

Securities that are classified as available-for-sale are measured at fair value with temporary unrealized gains and losses reported in other comprehensive loss, and as a component of stockholders' equity until their disposition. The Company reviews all available-for-sale securities at each period end to determine if they remain available-for-sale based on their current intent and ability to sell the security if it is required to do so. Realized gains and losses from the sale of marketable securities, if any, are calculated using the specific-identification method.

Marketable securities are subject to a periodic impairment review. The Company may recognize an impairment charge when a decline in the fair value of investments below the cost basis is determined to be other-than-temporary. In determining whether a decline in market value is other-than-temporary, various factors are considered, including the cause, duration of time and severity of the impairment, any adverse changes in the investees' financial condition, and the Company's intent and ability to hold the security for a period of time sufficient to allow for an anticipated recovery in market value. To date, there have been no declines in value deemed to be other than temporary for any of our investments in marketable securities.

Goodwill and Indefinite-Lived Intangible Asset

Goodwill and indefinite-lived intangible assets are reviewed for impairment at least annually in the fourth quarter, and more frequently if events or other changes in circumstances indicate that the carrying amount of the assets may not be recoverable. Impairment of goodwill and indefinite-lived intangibles is determined to exist when the fair value is less than the carrying value of the net assets being tested.

Goodwill

The difference between the purchase price and the fair value of assets acquired and liabilities assumed in a business combination is allocated to goodwill. Goodwill is evaluated for impairment on an annual basis as of October 1, and more frequently if indicators are present or changes in circumstances suggest that impairment may exist.

As of October 1, 2019 the Company has determined through its quantitative impairment test that the fair value of its goodwill significantly exceeded the carrying value of its single reporting unit, and concluded that goodwill was not impaired. The Company has not recognized any goodwill impairment in any of the periods presented.

Indefinite-Lived Intangible Asset

The Company's indefinite-lived intangible asset consists of IPR&D acquired in a business combination that are used in research and development activities but have not yet reached technological feasibility, regardless of whether they have alternative future use. The primary basis for determining the technological feasibility or completion of these projects is obtaining regulatory approval to market the underlying products in an applicable geographic region. The Company classifies IPR&D acquired in a business combination as an indefinite-lived intangible asset until the completion or abandonment of the associated research and development efforts. Upon completion of the associated research and development efforts, the Company performed a final test for impairment and will determine the useful life of the technology and begin amortizing the assets to reflect their use over their remaining lives. Upon permanent abandonment, the Company would write-off the remaining carrying amount of the associated IPR&D intangible asset.

Indefinite-lived intangible assets are not amortized, but instead are reviewed for impairment at least annually, or more frequently if events occur or circumstances change that would indicate the carrying amount may be impaired. In performing each annual impairment assessment and any interim impairment assessment, the Company determines if it should qualitatively assess whether it is more likely than not that the fair value of its IPR&D asset is less than its carrying amount (the qualitative impairment test). If the Company concludes that is the case, or elect not to use qualitative impairment test, the Company would proceed with quantitatively determining the fair value of the IPR&D asset and comparing its fair value to its carrying value to determine the amount of impairment, if any (the quantitative impairment test).

When performing the quantitative impairment assessment, the Company uses the income approach to determine the fair value of its IPR&D asset. This approach calculates fair value by estimating the after-tax cash flows attributable to an in-process project over its useful life and then discounting these after-tax cash flows back to a present value. This estimate includes judgmental assumptions regarding the estimates that market participants would make in evaluating the IPR&D asset, including the probability of successfully completing clinical trials and obtaining regulatory approval to market the IPR&D asset, the timing of and the expected costs to complete IPR&D projects, future net cash flows from potential drug sales, which are based on estimates of the sales price of the drug, the size of the patient population and cure rate, our competitive position in the marketplace, and appropriate discount and tax rates. Any impairment to be recorded is calculated as the difference between the fair value of the IPR&D asset as of the date of the assessment with the carrying value of the IPR&D asset on its consolidated balance sheet.

In performing the qualitative impairment test, the Company considers the results of the most recent quantitative impairment test and identifies the most relevant drivers of the fair value for the IPR&D asset. The most relevant drivers of fair value identified are consistent with the assumptions used in the quantitative estimate of the IPR&D asset discussed below. Using these drivers of fair value, the Company identifies events and circumstances that may have an effect on the fair value of the IPR&D asset since the last time the IPR&D's fair value was quantitatively determined. The Company then weighs these factors to determine and conclude if it is not more likely than not that

the IPR&D asset is impaired. If it is more likely than not that the IPR&D asset is impaired, the Company proceeds with quantitatively determining the fair value of the IPR&D asset.

For 2019, the Company elected to bypass the quantitative assessment and performed a qualitative impairment during the fourth quarter and concluded it is more likely than not the fair value of its IPR&D asset exceeded its carrying value and no further testing was required. The Company did not recognize any IPR&D impairment in any of the periods presented.

Leases

All of the Company's leases are operating leases for facilities and equipment. Prior to January 1, 2019, the Company recognized related rent expense on a straight-line basis over the term of the lease. Incentives granted under the Company's facilities lease, including allowances for leasehold improvements and rent holidays, were recognized as reductions to rental expense on a straight-line basis over the term of the lease. Deferred rent consisted of the difference between cash payments and the rent expense recognized.

Subsequent to the adoption of the new leasing standard on January 1, 2019, the Company recognizes a lease asset for its right to use the underlying asset and a lease liability for the corresponding lease obligation. The Company determines whether an arrangement is or contains a lease at contract inception. Operating leases with a duration greater than one year are included in operating lease right-of-use assets, operating lease liabilities - short-term, and operating lease liabilities - long-term in the Company's consolidated balance sheet at December 31, 2019. Operating lease right-of-use assets and liabilities are recognized at the lease commencement date based on the present value of lease payments over the lease term. In determining the net present value of lease payments, the Company uses its incremental borrowing rate based on the information available at the lease commencement date. The incremental borrowing rate represents the interest rate the Company would incur at lease commencement to borrow an amount equal to the lease payments on a collateralized basis over the term of a lease. The Company considers a lease term to be the noncancelable period that it has the right to use the underlying asset, including any periods where it is reasonably assured the Company will exercise the option to extend the contract. Periods covered by an option to extend are included in the lease term if the lessor controls the exercise of that option.

The operating lease right-of-use assets also include any lease payments made and exclude lease incentives. Lease expense is recognized on a straight-line basis over the expected lease term. Variable lease expenses are recorded when incurred. The Company has elected not to separate lease and non-lease components for its leased assets and accounts for all lease and non-lease components of its agreements as a single lease component.

Long-lived Assets

The Company monitors the carrying value of long-lived assets, including right-of-use operating lease assets, for potential impairment and tests the recoverability of such assets whenever events or changes in circumstances indicate that the carrying amounts may not be recoverable. If a change in circumstance occurs, the Company performs a test of recoverability by comparing the carrying value of the asset or asset group to its undiscounted expected future cash flows. If cash flows cannot be separately and independently identified for a single asset, the Company will determine whether impairment has occurred for the group of assets for which the Company can identify the projected cash flows. If the carrying values are in excess of undiscounted expected future cash flows, the Company measures any impairment by comparing the fair value of the asset or asset group to its carrying value. There were no indicators of impairment of long-lived assets for any periods presented.

Property and Equipment, Net

Property and equipment are stated at cost and consist of lab and office equipment, leasehold improvements and computer hardware and software. The Company records depreciation under the straight-line method over the estimated useful lives of its property and equipment ranging from three to seven years.

Leasehold improvements are amortized over the remaining terms of the respective leases or the estimated useful life of the leasehold improvements, whichever is less. Maintenance and repair costs are expensed as incurred.

Fair Value Measurements

The Company follows accounting guidance on fair value measurements for financial instruments measured on a recurring basis, as well as for certain assets and liabilities that are initially recorded at their estimated fair values. Fair value is defined as the exit price, or the amount that would be received from selling an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. The Company uses the following three-level hierarchy that maximizes the use of observable inputs and minimizes the use of unobservable inputs to value its financial instruments:

Level 1: Observable inputs such as unadjusted quoted prices in active markets for identical instruments.

Level 2: Quoted prices for similar instruments that are directly or indirectly observable in the marketplace.

Level 3: Significant unobservable inputs which are supported by little or no market activity and that are financial instruments whose values are determined using pricing models, discounted cash flow methodologies, or similar techniques, as well as instruments for which the determination of fair value requires significant judgment or estimation.

Financial instruments measured at fair value are classified in their entirety based on the lowest level of input that is significant to the fair value measurement. The assessment of the significance of a particular input to the fair value measurement in its entirety requires us to make judgments and consider factors specific to the asset or liability. The use of different assumptions and/or estimation methodologies may have a material effect on estimated fair values. Accordingly, the fair value estimates disclosed or initial amounts recorded may not be indicative of the amount that the Company or holders of the instruments could realize in a current market exchange.

The carrying amounts of cash equivalents and marketable securities approximate their fair value based upon quoted market prices. Certain of the Company's financial instruments are not measured at fair value on a recurring basis, but are recorded at amounts that approximate their fair value due to their liquid or short-term nature, such as cash, accounts receivable, accounts payable and accrued expenses.

The following tables present the fair value of the Company's financial assets measured at fair value on a recurring basis using the above input categories (in thousands):

	December 31, 2019			
	Level 1	Level 2	Level 3	Estimated Fair Value
Cash equivalents				
Money market funds	$ 33,095	$ —	$ —	$ 33,095
U.S. and foreign corporate debt securities	—	4,999	—	4,999
U.S. and foreign commercial paper	—	4,484	—	4,484
Total cash equivalents	33,095	9,483	—	42,578
Short-term investments				
U.S. and foreign corporate debt securities	—	72,486	—	72,486
Asset-backed securities	—	34,025	—	34,025
U.S. treasury securities	—	44,714	—	44,714
U.S. and foreign commercial paper	—	76,086	—	76,086
Total short-term investments	—	227,311	—	227,311
Total assets measured at fair value	$ 33,095	$ 236,794	$ —	$ 269,889

	December 31, 2018			
	Level 1	Level 2	Level 3	Estimated Fair Value
Cash equivalents				
Money market fund	$ 39,345	$ —	$ —	$ 39,345
Total cash equivalents	39,345	—	—	39,345
Short-term investments				
U.S. and foreign corporate debt securities	—	73,159	—	73,159
Asset-backed securities	—	28,419	—	28,419
U.S. treasury securities	—	19,895	—	19,895
U.S. and foreign commercial paper	—	55,136	—	55,136
Total short-term investments	—	176,609	—	176,609
Total assets measured at fair value	$ 39,345	$ 176,609	$ -	$ 215,954

The Company estimates the fair value of its U.S. and foreign corporate debt securities, asset backed securities, U.S. treasury securities and U.S. and foreign commercial paper by taking into consideration valuations obtained from third-party pricing services. The pricing services utilize industry standard valuation models, including both income and market-based approaches, for which all significant inputs are observable, either directly or indirectly, to estimate fair value. These inputs include reported trades of and broker/dealer quotes on the same or similar securities, issuer credit spreads; benchmark securities; prepayment/default projections based on historical data; and other observable inputs.

There have been no transfers between Level 1, Level 2 or Level 3 for any of the periods presented. See Note 3 for further information regarding the carrying value of our investments in marketable securities.

Revenue Recognition and Accounts Receivable from Collaboration

At the inception of an arrangement, we evaluate if a counterparty to a contract is a customer, if the arrangement is within the scope of revenue from contracts with customers guidance, and the term of the contract. We recognize revenue when the customer obtains control of promised goods or services in a contract for an amount that reflects the consideration we expect to receive in exchange for those goods or services. For contracts with customers, we apply the following five-step model in order to determine this amount: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations, including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) we satisfy each performance obligation. Our performance obligations under these arrangements may include licenses of intellectual property, options to license additional intellectual property, research and development services, delivery of manufactured product, and/or participation on joint steering committees. Allergan can select additional and/or back-up target indications to add to the licenses granted and also has the ability to enter into a contract manufacturing agreement with us for compound supply, and we have concluded that these rights are options. We evaluated whether such options contained material rights and concluded they were not offered at a discount that exceeds discounts available to other customers, and therefore were not material rights. The grant of additional licensing rights upon option exercises and contract manufacturing agreements will be accounted for as separate contracts when they occur.

We have provided standard indemnification and protection of licensed intellectual property for our customer. These provisions are part of assurance that the licenses meet the agreements, representations and are not obligations to provide goods or services.

We only apply the five-step model to contracts when it is probable that we will collect the consideration we are entitled to in exchange for the goods or services we transfer to the customer. As part of the accounting for contracts with customers, we must develop assumptions that require judgment to determine the standalone selling price of each performance obligation identified in the contract. We then allocate the total transaction price to each performance obligation based on the estimated standalone selling prices of each performance obligation. For the Allergan agreement, we estimated standalone selling prices of our performance obligations using income-based valuation approach for the estimated value a licensor of the compounds would receive. We recognize the amount of the transaction price that is allocated to the respective performance obligation when the performance obligation is satisfied or as it is satisfied as revenue. For our contract with Allergan, we recognize revenues for each of our distinct performance obligations as the related research and development services are performed because Allergan consumes the benefit of research and development work simultaneously as we perform these services.

Upfront License Fees

If a license to our intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, we recognize revenues from nonrefundable, upfront license fees based on the relative value prescribed to the license compared to the total value of the arrangement. The revenue is recognized when the license is transferred to the collaborator and the collaborator is able to use and benefit from the license. For licenses that are not distinct from other obligations identified in the arrangement, we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time. If the combined performance obligation is satisfied over time, we apply an appropriate method of measuring progress for purposes of recognizing revenue from nonrefundable, upfront license fees. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

Development and Regulatory Milestone Payments

Depending on facts and circumstances, we may record revenues from certain milestones in a reporting period before the milestone is achieved if we conclude that achievement of the milestone is probable and that recognition of revenue related to the milestone will not result in a significant reversal in amounts recognized in future periods. We record a corresponding contract asset when this conclusion is reached. Milestone payments that have not been included in the transaction price to date are fully constrained. We re-evaluate the probability of achievement of such milestones and any related constraint each reporting period. We adjust our estimate of the overall transaction price, including the amount of collaborative revenue that was recorded, if necessary.

Research and Development Service Payments

We are reimbursed at a certain percentage for performing research and development services based on hours worked by our employees, at a fixed contractual rate per hour, and third-party pass-through costs we incur on a quarterly basis. Research and development service payments are included in the transaction price in the reporting period that we conclude that it is probable that recording revenue in the period will not result in a significant reversal in amounts recognized in future periods. Accounts receivable are recorded when the right to the research and development service payment consideration becomes unconditional. We record the full reimbursed portion of these expenses as collaboration revenue in our consolidated statements of operations as we consider performing research and development services to be a part of our ongoing and central operations.

Sales-based Milestone and Royalty Payments

Our customer may be required to pay us sales-based milestone payments or royalties on future sales of commercial products. We recognize revenues related to sales-based milestone and royalty payments upon the later to occur of (i) achievement of the collaborator's underlying sales or (ii) satisfaction of any performance obligation(s) related to these sales, in each case assuming our licensed intellectual property is deemed to be the predominant item to which the sales-based milestones and/or royalties relate.

We receive payments from our customer based on billing schedules established in each contract. Upfront payments and fees are recorded as deferred revenue upon receipt or when due until we perform our obligations under the arrangement. If the related performance obligation is expected to be satisfied within the next twelve months, these amounts will be classified in current liabilities. We recognize a contract asset relating to our conditional right to consideration that is not subject to a constraint. Amounts are recorded as accounts receivable when our right to consideration is unconditional.

At December 31, 2019 and 2018, the accounts receivable recorded on the consolidated balance sheet relates to the Collaboration Agreement. All accounts receivable are deemed collectible. A net contract asset or liability is presented for each contract with a customer. We do not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the customer and the transfer of the promised goods or services to the customer will be one year or less.

Stock-Based Compensation

The Company measures stock-based compensation to employees, consultants, and Board members at fair value on the grant date of the award. The fair value of restricted stock units (RSUs) is determined based on the number of shares granted and the quoted market price of the Company's common stock on the date of grant. Compensation cost is recognized as expense on a straight-line basis over the requisite service period of the award. Stock-based awards with graded vesting schedules are recognized using the accelerated attribution method on a straight-line basis over the requisite service period for each separately vesting portion of the award. For awards that have a performance condition, compensation cost is measured based on the fair value of the award on the grant date, the date performance targets are established, and is expensed over the requisite service period for each separately vesting tranche when achievement of the performance condition becomes probable. We assess the probability of the performance conditions being met on a continuous basis. Forfeitures are recognized when they occur.

The Company estimates the fair value of stock option grants that do not contain market-based vesting conditions using the Black-Scholes option pricing model. The assumptions used in estimating the fair value of these awards, such as expected term, expected dividend yield, volatility and risk-free interest rate, represent management's best estimates and involve inherent uncertainties and the application of management's judgment. The Company is also required to make estimates as to the probability of achieving the specific performance conditions. If actual results are not consistent with the Company's assumptions and judgments used in making these estimates, the Company may be required to increase or decrease compensation expense, which could be material to the Company's consolidated results of operations.

Prior to the adoption of Accounting Standards Update (ASU) 2018-07 (ASU 2018-07) on January 1, 2019, the Company remeasured the fair value of the non-employee awards at each reporting period prior to vesting and finally at the vesting date of the award. Changes in the estimated fair value of these non-employee awards were recognized as compensation expense in the period of change. Subsequent to the adoption of ASU 2018-07, the Company recognizes non-employee compensation costs over the requisite service period based on a measurement of fair value for each stock award.

Research and Development Expense and Accruals

Research and development costs include personnel-related costs, outside contracted services including clinical study costs, facilities costs, fees paid to consultants, milestone payments prior to FDA approval, license fees prior to FDA approval, professional services, travel costs, dues and subscriptions, depreciation and materials used in clinical trials and research and development and costs incurred under the Collaboration Agreement. Research and development costs are expensed as incurred unless there is an alternative future use in other research and development projects. Payments made prior to the receipt of goods or services to be used in research and development are capitalized until the goods or services are received. Such payments are evaluated for current or long-term classification based on when they will be realized or consumed. Assets acquired as part of an asset acquisition that are used in research and development or are IPR&D are immediately expensed as research and development unless there is an alternative future use in other research and development projects.

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 contract research organizations (CROs) and manufacturing vendors that conduct and manage these activities on its behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract, and may result in uneven payment flows. There may be instances in which payments made to the Company's vendors will exceed the level of services provided and result in a prepayment of the expense. Payments under some of these contracts depend on factors such as the successful enrollment of subjects and the completion of clinical study milestones. In amortizing or accruing service fees, the Company estimates the time period over which services will be performed, enrollment of subjects, number of sites activated and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from the Company's estimate, the Company will adjust the accrued or prepaid expense balance accordingly. To date, there have been no material differences from the Company's estimates to the amounts actually incurred.

Income Taxes

The Company records income taxes using the asset and liability method. Deferred income tax assets and liabilities are recognized for the future tax effects attributable to temporary differences between the financial statement carrying amounts of existing assets and liabilities and their respective income tax bases, and operating loss and tax credit carryforwards. The effect of a change in tax rates on deferred tax assets and liabilities is recognized in income in the period that includes the enactment date. The Company establishes a valuation allowance if it is more likely than not that the deferred tax assets will not be realized based on an evaluation of objective verifiable evidence. For tax positions that are more likely than not of being sustained upon audit, the Company recognizes the largest amount of the benefit that is greater than 50% likely of being realized. For tax positions that are not more likely than not of being sustained upon audit, the Company does not recognize any portion of the benefit.

The Company recognizes and measures uncertain tax positions using a two-step approach set forth in authoritative guidance. The first step is to evaluate the tax position taken or expected to be taken by determining whether the weight of available evidence indicates that it is more likely than not that the tax position will be sustained in an audit, including resolution of any related appeals or litigation processes. The second step is to measure the tax benefit as the largest amount that is more than 50% likely to be realized upon ultimate settlement. Significant judgment is required to evaluate uncertain tax positions. The Company evaluates uncertain tax positions on a regular basis. The evaluations are based on a number of factors, including changes in facts and circumstances, changes in tax law, correspondence with tax authorities during the course of the audit, and effective settlement of audit issues. The provision for income taxes includes the effects of any accruals that the Company believes are appropriate. It is the Company's policy to recognize interest and penalties related to income tax matters in income tax expense. No interest or penalties related to uncertain tax positions has been incurred or accrued for any periods presented.

Net Loss per Share

Basic net loss per common share excludes dilution and is computed by dividing net loss by the weighted average number of common shares outstanding during the period. Diluted net loss per common share reflects the potential dilution that could occur if securities or other contracts to issue common stock were exercised or converted into common stock or resulted in the issuance of common stock that then shared in the earnings of the entity unless inclusion of such shares would be anti-dilutive. Since the Company has only incurred losses, basic and diluted net loss per share is the same.

The following table presents the potential common stock equivalents that were excluded from the computation of diluted loss from per share of common stock for the periods presented because including them would have been antidilutive:

	Year Ended December 31,		
	2019	**2018**	**2017**
Warrants to purchase common stock	15,296	15,296	15,296
Options to purchase common stock	5,613,353	4,637,145	4,551,819
Common stock subject to purchase under our ESPP	11,342	21,483	—
Unvested RSUs	630,384	568,005	120,000
Total	6,270,375	5,241,929	4,687,115

In December 2019, the Company sold 6,287,878 shares of common stock as well as 2,424,242 pre-funded warrants (see Note 6). The pre-funded warrants are exercisable for shares of common stock at a price of $0.001 per share. The shares of common stock into which the pre-funded warrants may be exercised are considered outstanding for the purposes of computing earnings per share because the shares may be issued for little or no consideration, they are fully vested, and are exercisable after the original issuance date.

Comprehensive Loss

Comprehensive loss is comprised of net loss and adjustments for the change in unrealized gains and losses on investments in available-for-sale marketable securities. The Company displays comprehensive loss and its components in the consolidated statements of operations and comprehensive loss, net of tax effects if any.

Concentrations of Risk

Credit Risk

Financial instruments which potentially subject the Company to credit risk consist primarily of cash, cash equivalents and marketable securities. The Company holds these investments in highly rated financial institutions, and, by policy, limits the amounts of credit exposure to any one financial institution. These amounts at times may exceed federally insured limits. The Company has not experienced any credit losses in such accounts and does not believe it is exposed to any significant credit risk on these funds. The Company has no off-balance sheet concentrations of credit risk, such as foreign currency exchange contracts, option contracts or other hedging arrangements.

Supplier Risk

Certain materials and key components the Company utilizes in its operations are obtained through single suppliers. Since the suppliers of key components and materials must be named in a New Drug Application (NDA) filed with the FDA for a product, significant delays can occur if the qualification of a new supplier is required. If delivery of material from the Company's suppliers were interrupted for any reason, the Company may be unable to supply any of its product candidates for clinical trials.

Adoption of Recent Accounting Pronouncements

On January 1, 2018, the Company adopted ASU No. 2014-09, *Revenue from Contracts with Customers*, as amended (Accounting Standards Codification Topic 6060) (ASC 606) using the modified retrospective method applied to those contracts which were not completed as of January 1, 2018. The Company also elected to use the practical expedient that allows an entity to expense the incremental cost of obtaining a contract as an expense when incurred if the amortization period of the asset that an entity otherwise would have recognized is less than one year. Results for the year ended December 31, 2019 and 2018 are presented under ASC 606, while prior period amounts are not adjusted and continue to be reported in accordance with historic accounting under previous revenue recognition guidance. As of the adoption date of ASC 606, the Company had only one contract with a customer, Allergan, that had not been completed. Based on the Company's analysis, the Company concluded there was no significant change in applying ASC 606 to the Collaboration Agreement and no amounts have been recognized within "accumulated deficit" in the consolidated balance sheet related to the adoption of the new standard.

In February 2016, the Financial Accounting Standards Board (FASB) issued ASU 2016-02, *Leases* (ASU 2016-02). Under this standard, which applies to both lessors and lessees, lessees will be required to recognize all leases (except for short-term leases) as a lease liability, which is a lessee's obligation to make lease payments arising from a lease measured on a discounted basis, and as a right-of-use asset, which is an asset that represents the lessee's right to use, or control the use of, a specified asset for the lease term. Leases will be classified as either financing or operating, with classification affecting the pattern of expense recognition in the income statement. In January, July and December 2018 and March 2019, the FASB issued additional amendments to the new lease guidance related to transition and clarification.

The Company adopted ASU 2016-02 on January 1, 2019 using the modified retrospective approach and elected the package of practical expedients permitted under transition guidance, which allowed the Company to carry forward its historical assessments of: (1) whether contracts are or contain leases, (2) lease classification and (3) initial direct costs. The Company did not elect the use-of-hindsight practical expedient, which would require the Company to reassess the lease term of its leases based on all facts and circumstances through the effective date, and the Company did not elect the practical expedient pertaining to land easements as this is not applicable to the Company's current contract portfolio. The Company elected the post-transition practical expedient to not separate lease components from nonlease components for all existing lease classes. The Company also elected a policy of not recording leases on its consolidated balance sheets when the leases have a term of 12 months or less and the Company is not reasonably certain to elect an option to purchase the leased asset.

The adoption of this standard resulted in the recognition of right of use (ROU) assets and lease liabilities of $13.8 million and $14.0 million, respectively, and the derecognition of the deferred rent balance of $0.1 million as of January 1, 2019. The adoption of the standard had no impact on the Company's consolidated statements of operations and comprehensive loss or to its cash flows from or used in operating, financing, or investing activities on its consolidated statements of cash flows. No cumulative-effect adjustment within accumulated deficit was required to be recorded as a result of adopting this standard.

On January 1, 2019, the Company adopted ASU 2018-02, *Income Statement - Reporting Comprehensive Income, (Topic 220): Reclassification of Certain Tax Effects from Accumulated Other Comprehensive Income,* which allows a reclassification from accumulated other comprehensive income to retained earnings for stranded tax effects resulting from the federal corporate income tax rate enacted under the Tax Cuts and Jobs Act (the Tax Act). The amount of the reclassification would be the difference between the historical corporate income tax rate and the Tax Act's 21% corporate income tax rate. The Company's adoption of this standard did not have a material impact on its consolidated financial statements.

On January 1, 2019, the Company adopted ASU 2018-07, *Compensation-Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting* (ASU 2018-07), which simplifies several aspects of the accounting for nonemployee share-based payment transactions resulting from expanding the scope of Topic 718, *Compensation – Stock Compensation* to include share-based payment transactions for acquiring goods and services from nonemployees. The Company's adoption of this standard did not have a material impact on its consolidated financial statements.

Accounting Pronouncements to Be Adopted

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments - Credit Losses: Measurement of Credit Losses on Financial Instruments* (ASU 2016-13), which requires that expected credit losses relating to financial assets measured on an amortized cost basis and available-for-sale debt securities be recorded through an allowance for credit losses. ASU 2016-13 limits the amount of credit losses to be recognized for available-for-sale debt securities to the amount by which carrying value exceeds fair value and also requires the reversal of previously recognized credit losses if fair value increases. In April, May and November 2019, the FASB issued additional amendments to the new guidance related to transition and clarification. In November 2019, the FASB issued ASU 2019-10, *Financial Instruments—Credit Losses (Topic 326), Derivatives and Hedging (Topic 815), and Leases (Topic 842): Effective Dates* (ASU 2019-10), which deferred the effective date of this standard for all entities except SEC filers that are not smaller reporting companies to fiscal years beginning after December 15, 2022, including interim periods within those fiscal years. Early adoption is permitted. The Company is currently evaluating the timing and impact of adopting this new accounting standard on its consolidated financial statements and related disclosures.

In January 2017, the FASB issued ASU 2017-04, *Intangibles-Goodwill and Other (Topic 350): Simplifying the Test for Goodwill Impairment* (ASU 2017-04), which simplifies how an entity is required to test goodwill for impairment by eliminating Step 2 from the goodwill impairment test. Step 2 measures a goodwill impairment loss by comparing the implied fair value of a reporting unit's goodwill with the carrying amount of that goodwill. Under the amendments in ASU 2017-04, an entity should recognize an impairment charge for the amount by which the carrying amount of a reporting unit exceeds its fair value; however, the loss recognized should not exceed the total amount of goodwill allocated to that reporting unit. The updated guidance requires a prospective adoption. In November 2019, the FASB issued ASU 2019-10, which deferred the effective date of this standard for all entities except SEC filers that are not smaller reporting companies to fiscal years beginning after December 15, 2022, including interim periods within those fiscal years. Early adoption is permitted for goodwill impairment tests performed on testing dates after January 1, 2017. The Company plans to adopt the standard on January 1, 2020 and does not expect the adoption of this guidance to have a material impact on its consolidated financial statements and related disclosures.

In August 2018, the FASB issued ASU 2018-13, *Fair Value Measurement (Topic 820): Disclosure Framework - Changes to the Disclosure Requirements for Fair Value Measurement,* which makes a number of changes meant to add, modify or remove certain disclosure requirements associated with the movement amongst or hierarchy associated with Level 1, Level 2 and Level 3 fair value measurements. This guidance is effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2019. The Company will adopt this ASU on January 1, 2020 and does not expect the adoption of this guidance to have a material impact on its consolidated financial statements and related disclosures.

In November 2018, the FASB issued ASU No. 2018-18, *Collaborative Arrangements (Topic 808): Clarifying the Interaction between Topic 808 and Topic 606* (ASU 2018-18), which clarifies that certain transactions between collaborative arrangement participants should be accounted for as revenue under the contract with customer guidance (Topic 606) when the collaborative arrangement participant is a customer in the context of a unit of account. In those situations, all the guidance in Topic 606 should be applied, including recognition, measurement, presentation, and disclosure requirements. The standard adds unit-of-account guidance in Topic 808 to align with the guidance in Topic 606 (that is, a distinct good or service) when an entity is assessing whether the collaborative arrangement or a part of the arrangement is within the scope of Topic 606, and requires that in a transaction with a

collaborative arrangement participant that is not directly related to sales to third parties, presenting the transaction together with revenue recognized under Topic 606 is precluded if the collaborative arrangement participant is not a customer. The standard is effective for interim and annual periods beginning after December 15, 2019, with early adoption permitted, including adoption in any interim period for public business entities for periods in which financial statements have not been issued. Amendments in the standard should be applied retrospectively to the date of initial application of Topic 606, but entities may elect to apply the amendments in Topic 808 retrospectively either to all contracts or only to contracts that are not completed at the date of initial application of Topic 606, and should disclose the election. An entity may also elect to apply the practical expedient for contract modifications that is permitted for entities using the modified retrospective transition method in Topic 606. The Company is still finalizing its analysis and evaluating the impact adopting this new accounting standard will have on its consolidated financial statements and related disclosures.

In December 2019, the FASB issued ASU No. 2019-12, *Simplifying the Accounting for Income Taxes*. The ASU eliminates certain exceptions to the guidance in ASC 740 related to the approach for intraperiod tax allocation, the methodology for calculating income taxes in an interim period and the recognition of deferred tax liabilities for outside basis differences. The new guidance also simplifies aspects of the accounting for franchise taxes and enacted changes in tax laws or rates and clarifies the accounting for transactions that result in a step-up in the tax basis of goodwill. The standard is effective for fiscal years beginning after December 15, 2020, and interim periods within those fiscal years. Early adoption is permitted in an interim or annual period. Entities that elect to early adopt the amendments in an interim period should reflect any adjustments as of the beginning of the annual period that includes that interim period. Additionally, entities that elect early adopting must adopt all the amendments in the same period. Entities will apply the guidance prospectively, except for certain amendments. The Company plans to early adopt the standard effective January 1, 2020 and does not expect the adoption of this guidance to have a material impact on its consolidated financial statements and related disclosures.

Note 3 - Investments in Marketable Securities

Investments in marketable available-for-sale securities consisted of the following (in thousands):

	December 31, 2019			
	Amortized Cost	Gross Unrealized Gain [1]	Gross Unrealized Loss [1]	Estimated Fair Value
Cash equivalents				
Money market funds	$ 33,095	$ —	$ —	$ 33,095
U.S. and foreign corporate debt securities	5,000	—	(1)	4,999
U.S. and foreign commercial paper	4,484	—	—	4,484
Total cash equivalents	42,579	—	(1)	42,578
Short-term investments				
U.S. and foreign corporate debt securities	72,452	38	(4)	72,486
Asset-backed securities	34,008	17	—	34,025
U.S. treasury securities	44,692	24	(2)	44,714
U.S. and foreign commercial paper	76,086	—	—	76,086
Total short-term investments	227,238	79	(6)	227,311
Total cash equivalents and investments	$ 269,817	$ 79	$ (7)	$ 269,889

	December 31, 2018			
	Amortized Cost	Gross Unrealized Gain [1]	Gross Unrealized Loss [1]	Estimated Fair Value
Cash equivalents				
Money market funds	$ 39,345	$ —	$ —	$ 39,345
Total cash equivalents	39,345	—	—	39,345
Short-term investments				
U.S. and foreign corporate debt securities	73,251	—	(92)	73,159
Asset-backed securities	28,450	—	(31)	28,419
U.S. treasury securities	19,898	—	(3)	19,895
U.S. and foreign commercial paper	55,136	—	—	55,136
Total short-term investments	176,735	-	(126)	176,609
Total cash equivalents and investments	$ 216,080	$ -	$ (126)	$ 215,954

[1] Gross unrealized gain (loss) is pre-tax.

As of December 31, 2019, the contractual term to maturity of short-term marketable securities held by the Company is less than one year. There were no long-term marketable securities held by the Company as of December 31, 2019.

Realized gains and losses for the years ended December 31, 2019, 2018 and 2017 were not significant. None of the Company's investments have been in a continuous unrealized loss position for more than 12 months as of December 31, 2019.

See Note 2 for further information regarding the fair value of our investments in marketable securities.

Note 4 - Property and Equipment, Net

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

	As of December 31,	
	2019	2018
Computer hardware and software	$ —	$ 194
Lab equipment	247	407
Office equipment	699	70
Leasehold improvement	2,084	790
Total property and equipment	3,030	1,461
Less: Accumulated depreciation	(1,200)	(1,057)
Construction in progress	—	153
Property and equipment, net	$ 1,830	$ 557

Depreciation expense for the years ended December 31, 2019, 2018 and 2017 was approximately $0.5 million, $0.6 million, and $0.2 million, respectively, and was recorded in both research and development expense and general and administrative expense in the consolidated statements of operations and comprehensive loss. Primarily all of property and equipment is located in the U.S.

Note 5 – Other Accrued Expenses

Other accrued expenses consist of the following (in thousands):

	As of December 31,	
	2019	2018
Other accrued expenses:		
Accrued compensation	$ 5,312	$ 5,011
Accrued restructuring charges	2,094	-
Accrued professional fees and other	880	1,107
Total other accrued expenses	$ 8,286	$ 6,118

In November 2019, the Company's Board of Directors approved the relocation of the Company corporate headquarters to South San Francisco, California which became effective January 1, 2020. The Company accrued restructuring charges of $2.1 million in 2019 related to one-time termination severance payments and other employee-related costs associated with the relocation plan. This represents the total amount expected to be incurred in connection with the relocation and is expected to be fully paid in 2020. Costs related to this relocation of $0.4 million are recorded in research and development expenses and $1.7 million in general and administrative expenses in the consolidated statement of operations and comprehensive loss at December 31, 2019.

Note 6 - Stockholders' Equity

The Company is authorized to issue 5,000,000 shares of preferred stock as of December 31, 2019 and 2018, respectively. As of December 31, 2019 and 2018, no shares of preferred stock were issued and outstanding. The Company is authorized to issue 100,000,000 shares of common stock as of December 31, 2019 and 2018, respectively.

Sale of Common Stock and Pre-Funded Warrants

In December 2017, the Company filed a registration statement on Form S-3 with the SEC using a "shelf" registration statement, file No. 333-222366, which became effective January 10, 2018 (the Registration Statement). Under this shelf registration process, the Company may from time to time sell any combination of the securities described in the Registration Statement in one or more offerings up to an aggregate offering price of $250.0 million. In connection with the filing of this Registration Statement, the Company entered into a sales agreement under which the Company may offer and sell shares of its common stock having an aggregate offering price of up to $75.0 million through "at the market offerings" (ATM). As of December 31, 2019, $21.4 million remains available for sale under this Registration Statement.

In November 2017, the Company sold to various investors an aggregate of 2,541,000 shares of common stock in a public offering at $27.25 per share, which included the exercise in full by the underwriters of their option to purchase 331,500 additional shares of common stock. The Company received aggregate net proceeds of $64.8 million from the offering and option exercise, after deducting underwriting discounts and commissions and offering expenses.

In July 2018, the Company sold to various investors an aggregate of 4,600,000 shares of common stock in a public offering at $36.00 per share, which included the exercise in full by the underwriters of their option to purchase 600,000 additional shares of common stock. The Company received aggregate net proceeds of approximately $155.4 million from the offering and the option exercise, after deducting underwriting discounts and commissions and offering expenses payable by the Company.

In December 2019, the Company sold to various investors an aggregate of 6,287,878 shares of common stock at a public offering price of $16.50 per share, which included the exercise in full by the underwriters of their option to purchase 1,136,363 shares of common stock, and pre-funded warrants to purchase 2,424,242 shares of common stock at a public offering price of $16.499. The Company received aggregate net proceeds of approximately $134.7 million from the offering and the option exercise, after deducting underwriting discounts and commissions and offering expenses payable by the Company. The pre-funded warrants are exercisable immediately upon issuance at an exercise price of $0.001 per share. Per their terms, the outstanding pre-funded warrants to purchase shares of the Company's common stock generally may not be exercised if the holder's ownership of the Company's common stock would exceed 19.99% following such exercise. The exercise price and number of shares of common stock issuable upon the exercise of the pre-funded warrants (Warrant Shares) are subject to adjustment in the event of any stock dividends and splits, reverse stock split, recapitalization, reorganization or similar transaction, as described in the pre-funded warrant agreements. Under certain circumstances, the pre-funded warrants may be exercisable on a "cashless" basis. In connection with the issuance and sale of the common stock and pre-funded warrants, the Company granted the pre-funded warrant holders certain registration rights with respect to the pre-funded warrants and the Warrant Shares.

The pre-funded warrants were classified as a component of permanent stockholders' equity within additional paid-in-capital and were recorded at the issuance date using a relative fair value allocation method. The pre-funded warrants are equity classified because they are freestanding financial instruments that are legally detachable and separately exercisable from the equity instruments, are immediately exercisable, do not embody an obligation for the Company to repurchase its shares, permit the holders to receive a fixed number of common shares upon exercise, are indexed to the Company's common stock and meet the equity classification criteria. In addition, such pre-funded warrants do not provide any guarantee of value or return. The Company valued the pre-funded warrants at issuance, concluding their sales price approximated their fair value, and allocated net proceeds from the sale proportionately to the common stock and pre-funded warrants of which $37.5 million allocated to the pre-funded warrants and recorded as a component of additional paid-in-capital.

Common Stock Warrants

As of December 31, 2019, the following warrants to purchase shares of the Company's common stock were issued and outstanding:

Issue date	Expiration date	Exercise price	Number of warrants outstanding
September 10, 2010	September 10, 2020	$ 30.00	15,296
December 16, 2019	None	$ 0.001	2,424,242
			2,439,538

There were no warrants exercised during the years ended December 31, 2019, 2018 and 2017. During the year ended December 31, 2018, 1,613 warrants to purchase common stock expired unexercised.

Note 7 - Stock-Based Compensation

Equity Incentive Plans

In May 2018, the Company's stockholders approved (1) the Assembly Biosciences, Inc. 2018 Stock Incentive Plan (the 2018 Plan) pursuant to which the Company reserved 1,900,000 shares of its common stock for issuance in connection with equity incentive awards and (2) the Assembly Biosciences, Inc. Employee Stock Purchase Plan (the 2018 ESPP).

In May 2019, the Company's stockholders approved an amendment to the 2018 Plan that increased the aggregate shares of common stock reserved under the 2018 Plan to 3,000,000.

As of December 31, 2019, the Company had awards outstanding under the following shareholder approved plans: 2010 Equity Incentive Plan (the 2010 Plan), which has been frozen; the Amended and Restated 2014 Stock Incentive Plan (the 2014 Plan); and the 2018 Plan. Shares of common stock underlying awards that are forfeited under the 2010 Plan on or after June 2, 2016 will become available for issuance under the 2014 Plan. As of December 31, 2019, the Company also had awards outstanding under the Assembly Biosciences, Inc. 2017 Inducement Award Plan and the 2019 Inducement Award Plan.

The Company issues new shares of common stock to settle options exercised or vested restricted stock units.

Stock Plan Activity

Stock Options

The following table summarizes the stock option activity and related information for 2019:

	Number of Shares	Weighted Average Exercise Price Per Share	Weighted Average Remaining Contractual Term (Years)	Total Intrinsic Value (in thousands)
Outstanding as of December 31, 2018	4,637,145	$ 17.21		
Granted	1,948,700	15.54		
Exercised	(585,292)	7.24		
Forfeited	(384,700)	42.92		
Expired	(2,500)	49.14		
Outstanding as of December 31, 2019	5,613,353	$ 15.90	7.253	$ 43,023
Exercisable as of December 31, 2019	3,096,631	$ 13.37	5.747	$ 31,391

The weighted-average grant-date fair value of options granted was $10.55, $30.84 and $17.37 during the years ended December 31, 2019, 2018 and 2017, respectively. The total intrinsic value of options exercised in 2019, 2018 and 2017 was $5.0 million, $31.1 million and $9.8 million, respectively.

RSUs

The following table summarizes RSU activity and related information for 2019:

	Number of RSU's	Weighted Average Fair Value Per RSU at Grant Price
Nonvested as of December 31, 2018	568,005	$ 37.18
Granted	465,428	15.19
Vested	(146,833)	39.14
Forfeited	(127,882)	24.38
Nonvested as of December 31, 2019	758,718 [(1)]	$ 25.47

(1) Includes 128,334 RSUs that have vested but are subject to deferred settlement, which have a weighted average remaining contractual term of 2.4 years.

The total fair value of RSUs vested and settled during 2019 and 2018 was $5.7 million and $5.3 million, respectively. The total intrinsic value of RSUs vested and settled during 2019 was $2.9 million. The total intrinsic value of RSUs vested and settled during 2018 was nominal. There were no RSUs vested and settled in 2017.

As of December 31, 2019, RSUs outstanding include 45,000 granted in December 2017 and 100,000 granted in September 2019, each with performance-based conditions to executives of the Company. In the second quarter of 2019, 100,000 RSUs granted to a former officer were forfeited due to his departure. These RSUs had a grant date fair value of $2.4 million and were vesting over time but would have accelerated upon the achievement of certain performance-based conditions. The Company reversed the previously recognized expense of $0.5 million related to these forfeited awards upon the departure of the former officer.

Employee Stock Purchase Plan

The 2018 ESPP provides for the purchase by employees of up to an aggregate of 400,000 shares of the Company's common stock at a discount to the market price. Subject to the annual statutory limits and the 2018 ESPP's limit of 1,000 shares of common stock per offering, an eligible employee may participate through payroll deductions of up to 15% of such employee's compensation for each pay period

Eligible employees can purchase the Company's common stock at the end of a predetermined offering period at 85% of the lower of the fair market value at the beginning or end of the offering period. Under the 2018 ESPP, the offering periods end on the last business day occurring on or before May 14 or November 14. The ESPP is compensatory and results in stock-based compensation expense.

In November 2018, employees purchased 21,483 shares of common stock under the 2018 ESPP. In May and November 2019, employees purchased 36,804 and 22,566 shares of common stock, respectively, under the 2018 ESPP. As of December 31, 2019, 319,147 shares of common stock are available for future sale under the Company's 2018 ESPP. Stock-based compensation expense recorded in connection with the 2018 ESPP was approximately $0.4 million and $0.2 million for the years December 31, 2019 and 2018, respectively.

Valuation Assumptions

The Company used the Black-Scholes option-pricing model for determining the estimated fair value and stock-based compensation related to stock options and ESPP purchase rights.

A summary of the assumptions used to estimate the fair values of stock options grants for the years presented is as follows:

	Year Ended December 31,		
	2019	**2018**	**2017**
Exercise price	$9.31 - $23.04	$23.78 - $57.53	$21.81 - $44.28
Expected volatility	66.45% - 83.23%	75.6% - 86.1%	81.2% - 87.0%
Risk-free interest rate	1.36% - 2.65%	2.56% - 3.04%	2.02% - 2.29%
Expected term (years)	5.5 - 7.5	5.5 - 7.0	5.5 - 7.0
Expected dividend yield	-	-	-

The risk-free interest rate assumption was based on the rates for U.S. Treasury zero-coupon bonds with maturities similar to those of the expected term of the stock option being valued. The expected dividend yield was zero as the Company currently does not intend to pay dividends in the foreseeable future. The weighted average expected term of options was calculated using the simplified method as prescribed by accounting guidance for stock-based compensation due to the Company's limited history of relevant stock option exercise activity. The expected volatility was calculated based on the Company's historical stock prices, supplemented as necessary with historical volatility of the common stock of several peer companies with characteristics similar to those of the Company.

The fair value of ESPP purchase rights were not material for any period presented.

Stock-Based Compensation Expense

The Company recognized stock-based compensation expense included in the consolidated statement of operations and comprehensive loss for the periods presented (in thousands):

	Year Ended December 31,		
	2019	**2018**	**2017**
Research and development	$ 11,376	$ 11,820	$ 5,423
General and administrative	9,182 [(1)]	16,665	3,178
Total stock-based compensation expense	**$ 20,558**	**$ 28,485**	**$ 8,601**

(1) Includes the reversal of previously recognized expense of $3.6 million related to forfeited awards resulting from the departure of one of our former executive officers during the year.

As of December 31, 2019, there was approximately $27.5 million of total unrecognized stock-based compensation related to outstanding equity awards which is expected to be recognized over a weighted average remaining amortization period of 1.7 years.

Note 8 - Collaboration Agreement

Allergan

In January 2017, the Company entered into the Collaboration Agreement with Allergan to develop and commercialize select microbiome gastrointestinal disease therapies. Pursuant to the Collaboration Agreement, the Company granted Allergan an exclusive worldwide license to certain of its intellectual property, including its intellectual property arising under the Collaboration Agreement, to develop and commercialize licensed compounds for ulcerative colitis (UC), Crohn's disease, and two compounds for irritable bowel syndrome (IBS). Allergan and the Company also agreed to collaborate on research and development activities with respect to the licensed compounds in accordance with a mutually agreed upon research and development plan. Per the terms of the Collaboration Agreement, Allergan can select backups and additional target indications to add to the licenses granted for additional consideration and also have the ability to enter into a contract manufacturing agreement with the Company for compound supply at cost plus an agreed upon margin. In addition, the Company will participate on a Joint Development Committee (JDC) and Joint Patent Committee (JPC). The Company provided to Allergan standard indemnification and protection of licensed intellectual property, which is part of assurance that the license meets the contract's specifications and is not an obligation to provide goods or services.

Allergan paid the Company an upfront non-refundable payment of $50.0 million which was received in 2017. Additionally, the Company is eligible to receive variable consideration in the form of research and development cost reimbursements, up to approximately $631.0 million related to seven development milestones and up to approximately $2.14 billion related to 12 commercial development and sales milestones in connection with the successful development and commercialization of licensed compounds. In addition, the Company is eligible to receive tiered royalties at rates ranging from the mid-single digits to the mid-teens based on net sales.

Allergan and the Company have agreed to share research and development costs up to an aggregate of $75.0 million through proof-of-concept (POC) studies on a ⅔, ⅓ basis, respectively, and Allergan has agreed to assume all post-POC development costs. In the event any pre-POC development costs exceed $75.0 million in the aggregate, the Company may elect either (a) to fund ⅓ of such costs in excess of $75.0 million or (b) to allow Allergan to deduct from future development milestone payments ⅓ of the development costs funded by Allergan in excess of $75.0 million plus a premium of 25%. The Company has an option to co-promote the licensed programs in the U.S. and China, subject to certain conditions set forth in the Collaboration Agreement.

Allergan may terminate the Collaboration Agreement at any time upon either 90 days' (prior to the initiation of the first POC trial of a licensed product) or 120 days' (after the initiation of the first POC trial of a licensed product), as applicable, advance written notice to the Company. Unless terminated early, the Collaboration Agreement has a term that ends on the earlier of the (i) the period when POC studies have been completed and no further licensed compounds are in development (ii) expiration of the last to exist valid claim covering the manufacture, use and sale of the licensed compounds. The Collaboration Agreement also contains customary provisions for termination by either party, including in the event of breach of the Collaboration Agreement, subject to cure. Upon termination for convenience, the license and know how all revert to the Company.

The Company concluded that Allegan is a customer, and the contract is not subject to accounting literature on collaborative arrangements. This is because the Company granted to Allergan licenses to its intellectual property and agreed to perform research and development services, all of which are outputs of the Company's ongoing activities, in exchange for consideration. The Company identified the following material promises under the Collaboration Agreement: 1) transfer of a licenses to intellectual property for the four initial indications, inclusive of the related technology know-how (Licenses); 2) the obligation to perform research development services through POC (Development Services). The Company's participation on the JDC and JPC were considered to be immaterial in the context of the contract. The Company's co-promotion option was not considered to be a performance obligation. Allergan's selection of backups or additional target indications to add to the licenses granted for additional consideration and ability to enter into a contract manufacturing agreement with the Company for compound supply at cost plus an agreed upon margin were not considered to be performance obligations as the Company concluded the options were not offered at a discount that exceeds discounts available to other customers, and therefore were not material rights. The grant of additional licensing rights upon option exercises and contract manufacturing agreements will be accounted for as separate contracts when they occur.

The Company concluded the Licenses each were considered to be functional as they have significant standalone functionality and were capable of being distinct. However, the Company determined that each of the Licenses individually were not distinct from the Development Services within the context of the agreement. This is because Allergan is dependent on the Company to execute the Development Services, that it is only uniquely able to perform, in order for Allergan to benefit from the Licenses. As such, The Company determined that it has four performance obligations under the Collaboration Agreement associated with the transfer of the four compound Licenses combined with the performance of the Development Services for each of the four compound indications. The Company determined that the four performance obligations will be performed over the duration of the contract, which began in February 2017 and ends upon completion of the Development Services which is currently estimated to occur in 2025. The Company is using a cost-based input method to measure proportional performance and to calculate the corresponding amount of revenue to recognize. The Company believes this is the best measure of progress because other measures do not reflect how the Company transfers its performance obligation to Allegan. In applying the cost-based input method of revenue recognition, the Company measures costs incurred relative to budgeted costs to fulfill the four performance obligations. These costs consist primarily of third-party contract costs and internal labor costs. Revenue will be recognized based on actual costs incurred as a percentage of total budgeted costs as the Company completes its performance obligations.

To allocate transaction price among the four performance obligations, the Company estimated their standalone selling price (SSP) using income-based valuation approach for the estimated value a licensor of the compounds would receive considering the stage of the compounds development. The Company believes that a change in the assumptions used to determine its best estimate of selling price for the four performance obligations would not have a significant effect on the allocation of consideration received to the four performance obligations.

The transaction price at the inception of the agreement, was limited to $50.0 million upfront payment. Of this amount, the Company allocated $12.5 million to each of the four performance obligations. Research and development cost reimbursement payments are included in the transaction price in the reporting period that the Company concludes that it is probable that recording revenue in the period will not result in a significant reversal in amounts recognized. The variable consideration related to the remaining development and commercialization milestone payments has not been included in the transaction price as these were fully constrained at December 31, 2019. As part of the Company's evaluation of the development and commercialization milestones constraint, the Company determined the achievement of such milestones are contingent upon success in future clinical trials and regulatory approvals which are not within its control and uncertain at this stage. Any variable consideration related to sales-based milestones (including royalties) will be recognized when the related sales occur as they were determined to relate predominantly to the license granted to Allergan. The Company reevaluates the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

The Company did not incur any significant incremental costs of obtaining the Allergan contract.

For the year ended December 31, 2019 and 2018, the Company recorded approximately $16.0 million and $14.8 million, respectively, in revenue associated with the Collaboration Agreement. Short-term and long-term deferred revenue contract liabilities related to the Collaboration Agreement were approximately $6.4 million and approximately $30.6 million at December 31, 2019 and approximately $5.1 million and approximately $35.6 million at December 31, 2018.

On the consolidated balance sheets, contract asset balances of approximately $3.4 million and approximately $2.4 million were recorded as accounts receivable from collaboration as of December 31, 2019 and 2018, respectively.

The following tables present changes in the Company's contract liabilities and sources of collaboration revenue recognized during each period (in thousands):

	Balance at Beginning of Period	Additions	Deductions	Balance at End of Period
Year Ended December 31, 2019				
Contract liabilities:				
Deferred revenue	$ 40,660	$ —	$ (3,612)	$ 37,048
Year Ended December 31, 2018				
Contract liabilities:				
Deferred revenue	$ 45,785	$ —	$ (5,125)	$ 40,660

	Year Ended December 31,	
	2019	2018
Collaboration revenue recognized in the period from		
Amounts included in deferred revenue at the beginning of the period	3,612	5,125
Performance obligations satisfied in previous periods	—	—

Note 9 - Milestones and Research Agreements

HBV Research Agreement with Indiana University

Since September 2013, the Company has been party to an exclusive License Agreement dated September 3, 2013 with Indiana University Research and Technology Corporation (IURTC) from whom it has licensed aspects of the Company's HBV program held by IURTC. The license agreement requires the Company to make milestone payments based upon the successful accomplishment of clinical and regulatory milestones. The aggregate amount of all performance milestone payments under the IURTC license agreement, should all milestones through development be met, is approximately $0.8 million, with a portion related to the first performance milestone having been paid. The Company also is obligated to pay IURTC royalty payments based on net sales of the licensed technology. The Company is also obligated to pay diligence maintenance fees each year to the extent that the royalty, sublicensing, and milestone payments to IURTC are less than the diligence maintenance fee for that year. The Company made approximately $0.1 million in milestone payments for the year ended December 31, 2018. No milestone payments were incurred or accrued for under this agreement as of and for the years ended December 31, 2019 or 2017.

Microbiome Targeted Colonic Delivery Platform

In November 2013, the Company entered into a License and Collaboration Agreement with Therabiome, LLC (Therabiome), for all intellectual property and know-how owned or controlled by Therabiome relating to the oral delivery of pharmaceutical drugs to specific sites in the intestine, using a pH sensitive controlled release capsule-in-capsule technology. The Company will be solely responsible for all research and development activities with respect to any product it develops under the license.

The Company must pay Therabiome clinical and regulatory milestones for each product or therapy advanced from the platform for U.S. regulatory milestones. The Company also must pay Therabiome lesser amounts for foreign regulatory milestones, which vary by country and region. The Company also must pay Therabiome royalties on annual net sales of a product in the low to mid-single digit percentages plus, once annual net sales exceed certain thresholds, a one-time cash payment upon reaching the thresholds.

Therabiome must pay the Company royalties on annual net sales of any product Therabiome is permitted to develop using the intellectual property in the low double to mid-double digit percentages, depending on the level of development or involvement the Company had in the product. Two regulatory milestones resulting in payments totaling $0.4 million were determined to have occurred under this agreement and were paid in the year ended

December 31, 2019. No amounts were incurred or accrued for this agreement as of and for the years ended December 31, 2018 and 2017.

Note 10 - Income Taxes

There was no current income tax provision for the years ended December 31, 2019, 2018 and 2017. The Company recognized deferred income tax benefit of $0.8 million and $9.1 million for the years ended December 31, 2019 and 2017, respectively, and deferred income tax expense of $1.1 million for the year ended December 31, 2018.

The effective tax rate of our provision for income taxes differs from the federal statutory rate as follows:

	As of December 31,		
	2019	**2018**	**2017**
Statutory federal income tax rate	21.0%	21.0%	34.0%
State taxes, net of federal tax benefit	5.6	7.1	2.6
Stock based compensation	(3.8)	6.7	0.0
Research and development tax credits	5.6	2.4	2.1
Effective change in enacted tax rates	—	—	(47.7)
State rate change	(1.4)	2.5	(0.2)
Uncertain tax positions	(2.1)	(4.8)	—
Return to provision adjustments	(2.5)	4.4	—
Other	(0.2)	0.8	(0.3)
Change in valuation allowance	(21.4)	(41.3)	27.0
Income taxes provision (benefit)	0.8%	(1.2)%	17.5%

Significant components of the Company's deferred taxes are as follows (in thousands):

	As of December 31,	
	2019	2018
Deferred tax assets:		
Federal and state-operating loss carryforwards	$ 81,584	$ 58,668
Stock-based compensation	12,347	14,023
Intangible assets	1,774	2,282
Deferred revenue	9,503	11,409
Operating lease liabilities	3,147	—
Research and development credits	7,499	5,472
Other	702	575
Total deferred tax assets	116,556	92,429
Valuation allowance	(108,577)	(87,543)
Deferred tax asset, net of valuation allowance	$ 7,979	$ 4,886
Deferred tax liabilities:		
In-process research and development	$ (7,439)	$ (8,138)
Operating lease right-of-use assets	(3,071)	—
Total deferred tax liabilities	(10,510)	(8,138)
Net deferred tax liability	$ (2,531)	$ (3,252)

The Company maintains a valuation allowance on deferred tax assets due to the uncertainty regarding the ability to utilize these deferred tax assets in the future. The in-process research and development deferred tax liability was recorded in connection with the merger with Assembly Pharmaceuticals, Inc. in 2014 and relates to the difference between the carrying amount of in-process research and development for financial statement purposes relative to the amount used for income tax purposes.

On December 22, 2017, the Tax Act, was signed into law. Among other items, the Tax Act reduces the federal corporate tax rate to 21% from the existing applicable rate of 34%, effective January 1, 2018. As a result, in 2017 the Company recorded a decrease to its deferred tax assets of $24.7 million and to valuation allowance of $28.4 million, resulting in a net tax benefit of $3.7 million.

The Tax Act also permits an indefinite carry forward of net operating losses generated in taxable years ending after December 31, 2017, subject to a utilization limitation of 80% of taxable income. Due to the change in the carryforward period for post-2017 net operating losses, the Company determined that it would be able to use the deferred tax liability associated with certain in-process research and development as a source of income in determining the realizability of its deferred tax assets. As a result, in 2017 the Company recorded a $4.9 million income tax benefit from the reduction of its valuation allowance.

On December 22, 2017, Staff Accounting Bulletin No. 118, or SAB 118, was issued to address the application of GAAP in situations when a registrant does not have the necessary information available, prepared, or analyzed (including computations) in reasonable detail to complete the accounting for certain income tax effects of the Act. The Company was able to provide a reasonable estimate for the revaluation of deferred taxes. The Company completed its review in December 2018 with no material adjustments to the provisional amount previously recorded.

The Company's income tax benefit for the year ended December 31, 2017 of $9.1 million includes a tax benefit of $8.6 million related to the Tax Act.

As of December 31, 2019, the Company had potentially utilizable gross federal net operating loss carryforwards of approximately $297.6 million with $182.9 million of net operating losses that carry forward indefinitely and $114.7 million of net operating losses which begin to expire in 2027. There are state net operating loss carryforwards of $309.3 million with $1.0 million carrying forward indefinitely and $308.3 million beginning to expire in 2031. In addition, the Company has federal research and development credit carryforwards of approximately $9.0 million which begin to expire in 2028 if not utilized and California research and development credit carryforwards of $5.3 million, which will carryforward indefinitely.

Pursuant to Internal Revenue Code (IRC), Section 382 and 383, use of the Company's U.S. federal and state net operating loss and research and development income tax credit carryforwards may be limited in the event of a cumulative change in ownership of more than 50.0% within a three-year period. The Company has performed an ownership change study through December 31, 2018 and has determined that a "change in ownership" as defined by IRC Section 382 and the rules and regulations promulgated thereunder, did occur in December 2010, January 2013 and October 2014. The Company has adjusted its net operating loss carryovers to appropriately reflect any attributes which will expire due to the limitation. The Company has not performed any additional analysis for IRC Sections 382 and 383 and there is a risk that additional changes in ownership could have occurred since December 31, 2018. If a change in ownership were to have occurred, additional net operating loss and tax credit carryforwards could be eliminated or restricted. If eliminated, the related asset would be removed from the deferred tax asset schedule with a corresponding reduction in the valuation allowance.

The following table summarizes activity related to the Company's gross unrecognized tax benefits (in thousands):

	Total
Balances as of December 31, 2017	$ —
Increases related to prior year tax positions	3,679
Increases related to 2018 tax positions	934
Balances as of December 31, 2018	$ 4,613
Increases related to prior year tax positions	15
Decreases related to prior year tax positions	(934)
Increases related to 2019 tax positions	2,376
Balances as of December 31, 2019	$ 6,070

The unrecognized tax benefits, if recognized, would not have an impact on the Company's effective tax rate assuming the Company continues to maintain a full valuation allowance position. Based on prior year's operations and experience, the Company does not expect a significant change to its unrecognized tax benefits over the next twelve months. The unrecognized tax benefits may increase or change during the next year for unexpected or unusual items for items that arise in the ordinary course of business. In subsequent periods, any interest and penalties related to uncertain tax positions will be recognized as a component of income tax expense.

The Company files income tax returns in the U.S. federal and other state jurisdictions and is not currently under examination by federal, state, or local taxing authorities for any open tax years. Due to net operating loss carryforwards, all years effectively remain open for income tax examination by tax authorities in the U.S. and states in which the Company files tax returns.

Note 11 - Leases

Operating Leases

The Company leases corporate office and laboratory space in South San Francisco, California under a sub-sublease that expires in December 2023. The Company also leases office space for administrative functions in Carmel, Indiana under a lease agreement that expires in August 2023. Prior to moving into the South San Francisco office and laboratory space in February 2019, the Company leased office and laboratory space in San Francisco, California, under a sublease that expired in February 2019. The Company also leases office and laboratory space in Groton, Connecticut under a lease that expires in March 2021. The Company's China subsidiary leases office space and lab space in Shanghai that expires in December 2020. Additionally, the Company's China subsidiary leases office space in Beijing under a lease agreement that expires in December 2020. Certain lease contracts contain renewal clauses that the Company assesses on a case by case basis. The Company also leases certain laboratory equipment accounted for as operating leases. These equipment leases began to expire in 2017, with the final lease expiring in 2022.

When the Company cannot determine the implicit rate in its leasing arrangements, the Company uses its incremental borrowing rate as the discount rate when measuring operating lease liabilities. The incremental borrowing rate represents an estimate of the interest rate the Company would incur at lease commencement to borrow an amount

equal to the lease payments on a collateralized basis over the term of a lease within a particular currency environment.

At December 31, 2019, the Company had operating lease liabilities of $12.3 million and right-of-use assets of $12.0 million, which were included in the consolidated balance sheet.

The following summarizes quantitative information about the Company's operating leases for the year ended December 31, 2019 (in thousands):

Lease cost		
Operating lease cost	$	4,454
Short-term lease cost		609
Variable lease cost		1,193
Total lease cost	$	6,256
Operating cash flows from operating leases	$	4,268
Right-of-use assets exchanged for new operating lease liabilities	$	1,328

As of December 31, 2019, the weighted-average remaining lease term for operating leases was approximately 2.7 years and the weighted-average discount rate for operating leases was approximately 9.4%.

As of December 31, 2019, the maturities of the Company's operating lease liabilities were as follows (in thousands):

2020	4,583
2021	3,791
2022	3,438
2023	3,303
Total	15,115
Less: present value discount	(2,847)
Operating lease liabilities	$ 12,268

Operating lease costs were approximately $6.3 million, $4.2 million and $2.1 million for the years ended December 31, 2019, 2018 and 2017, respectively.

Note 12 - Employee Benefit Plan

In January 2018, the Company established a defined contribution 401(k) plan (the Plan) for all employees who are at least 21 years of age. Employees are eligible to participate in the Plan upon commencement of employment. Under the terms of the Plan, employees may make voluntary contributions as a percentage of compensation. The Plan also permits the Company to make discretionary matching contributions. In 2019 and 2018, the Company made discretionary matching contributions of $0.7 million and $0.7 million, respectively.

In 2017, the Company participated in a professional employer organization sponsored 401(k) plan. The Company did not make any discretionary matching contributions in 2017.

Note 13 - Selected Quarterly Financial Data (Unaudited)

The following table contains quarterly financial information for the four quarters of 2019 and 2018 which has been prepared in accordance with GAAP for interim financial information. The Company believes that the following information reflects all normal recurring adjustments necessary for a fair statement of the information for the periods presented.

	2019 Quarter Ended			
	March 31	June 30	September 30	December 31
	(in thousands except for per share amounts)			
Collaboration revenue	$ 3,885	$ 3,080	$ 4,231	$ 4,767
Operating expenses	$ 32,221	$ 22,780	$ 30,224	$ 33,451
Interest and other income	$ 1,276	$ 1,182	$ 983	$ 859
Unrealized gain (loss) from marketable securities, net of tax	$ 108	$ 52	$ (18)	$ 4
Net loss	$ (27,052)	$ (18,503)	$ (24,995)	$ (27,084)
Basic and diluted net loss per common share	$ (1.05)	$ (0.72)	$ (0.96)	$ (0.99)

	2018 Quarter Ended			
	March 31	June 30	September 30	December 31
	(in thousands except for per share amounts)			
Collaboration revenue	$ 3,565	$ 3,218	$ 4,286	$ 3,735
Operating expenses	$ 20,237	$ 30,384	$ 26,861	$ 30,057
Interest and other income	$ 446	$ 453	$ 1,116	$ 1,069
Unrealized gain (loss) from marketable securities, net of tax	$ (23)	$ (127)	$ (82)	$ 231
Net loss	$ (16,249)	$ (26,806)	$ (21,535)	$ (26,161)
Basic and diluted net loss per common share	$ (0.80)	$ (1.30)	$ (0.87)	$ (1.03)

CORPORATE INFORMATION

Directors

Anthony E. Altig
Former Chief Financial Officer, Biotix Holdings, Inc.

Mark Auerbach
Former Non-Executive Chairman of the Board and Chairman of the Audit Committee for RCS Capital Corporation; Former Lead Independent Director and Chairman of the Audit Committee of Optimer Pharmaceuticals, Inc.

Richard D. DiMarchi, Ph.D.
Cox Distinguished Professor of Biochemistry and Gill Chair in Biomolecular Sciences and

Myron Z. Holubiak
President and Chief Executive Officer, Citius Pharmaceuticals, Inc.

Helen S. Kim
Managing Director, Vida Ventures

Alan J. Lewis, Ph.D.
Former Chief Executive Officer, DiaVacs, Inc.

Susan Mahony, Ph.D.
Former Senior Vice President and President of Lilly Oncology, Eli Lilly and Company

John G. McHutchison, A.O., M.D.
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