UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2017

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 No. 001-38359

resTORbio, Inc.

(Exact name of registrant as specified in its charter)

Delaware **(State or other jurisdiction of incorporation or organization)**	**81-3305277** **(I.R.S. Employer Identification No.)**

500 Boylston Street, 12th Floor
Boston, MA 02116
(857) 315-5521

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

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

Title of each class	**Name of each exchange on which registered**
Common Stock, par value $0.0001 per share	**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 15(d) of the Act. ☐ Yes ☒ No

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. ☐ Yes ☒ No

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). ☒ Yes ☐ No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☒

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

Large accelerated filer ☐	Accelerated filer ☐	Non-accelerated filer ☒ (Do not check if a smaller reporting company)	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 7(a)(2)(B) of the Securities 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 registrant's common stock began trading on The Nasdaq Global Select Market on January 26, 2018. As of March 23, 2018, the aggregate market value of the registrant's voting and non-voting common stock held by non-affiliates (without admitting that any person whose shares are not included in such calculation is an affiliate) computed by reference to the price at which the common stock was last sold on March 23, 2018 was approximately $113.6 million. The registrant has provided this information as of March 23, 2018 because the registrant was not a public company as of the last business day of its most recently completed second fiscal quarter and therefore cannot calculate the aggregate market value of its voting and non-voting equity held by non-affiliates as of such date.

As of March 23, 2018 there were 28,046,315 shares of common stock, $0.0001 par value per share, outstanding.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This Annual Report on Form 10-K contains forward-looking statements that 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 revenue, projected costs, prospects, plans and objectives of management and expected market growth are forward-looking statements. The words “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “would” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

These forward-looking statements include, among other things, statements about:

- our plans to develop and commercialize RTB101 alone or in combination with everolimus and other product candidates, including the therapeutic potential and clinical benefits thereof;
- our ongoing and future clinical trials for RTB101 alone or in combination with everolimus, whether conducted by us or by any future collaborators, including the timing of initiation of these trials and of the anticipated results;
- the timing of and our ability to obtain and maintain regulatory approvals for our product candidates;
- the rate and degree of market acceptance and clinical utility of any products for which we receive regulatory approval;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our intellectual property position and strategy;
- our ability to identify additional product candidates with significant commercial potential;
- our plans to enter into collaborations for the development and commercialization of product candidates;
- the potential benefits of any future collaboration;
- our expectations related to the use of proceeds from our initial public offering;
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- developments relating to our competitors and our industry; and
- the impact of government laws and regulations.

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. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, collaborations, joint ventures or investments that we may make or enter into.

You should read this Annual Report on Form 10-K and the documents that we reference herein and have filed or incorporated by reference as exhibits hereto 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.

This Annual Report on Form 10-K includes statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. We are responsible for all of the disclosure contained in this Annual Report on Form 10-K, and we believe these industry publications and third-party research, surveys and studies are reliable.

PART I

Unless the context requires otherwise, references in this Annual Report on Form 10-K to the "Company," "resTORbio," "we," "us," and "our" refer to resTORbio, Inc. Our "board of directors" refers to the board of directors of resTORbio, Inc.

Item 1. Business.

Overview

We are a clinical-stage biopharmaceutical company focused on the development and commercialization of novel therapeutics for the treatment of aging-related diseases. Our lead program has demonstrated in several clinical trials, including a randomized, placebo-controlled trial, the potential to treat multiple diseases of aging for which there are no approved therapies. The decline in immune function that occurs during aging, or immunosenescence, increases susceptibility to a variety of diseases, including respiratory tract infections, or RTIs, that significantly contribute to morbidity and mortality in the elderly. Our approach focuses on the mechanistic target of rapamycin, or mTOR, pathway, an evolutionarily conserved pathway that regulates aging, and specifically on selective inhibition of the target of rapamycin complex 1, or TORC1. Our initial focus is on the development of RTB101, an orally administered, small molecule, potent TORC1 inhibitor, alone and in combination with other mTOR inhibitors such as everolimus—as a first-in-class immunotherapy program designed to improve immune function and thereby reduce the incidence of RTIs in the elderly regardless of the causative pathogen. We licensed the worldwide rights to our TORC1 program, including RTB101 alone or in combination with everolimus or other mTOR inhibitors, from Novartis International Pharmaceutical Ltd., or Novartis, in March 2017.

Our TORC1 immunotherapy approach is supported by a randomized, placebo-controlled Phase 2a clinical trial in 264 elderly subjects that provided statistically significant and clinically meaningful results. This trial demonstrated that treatment with RTB101 alone and in combination with everolimus can enhance the ability of the aging immune system to fight infectious pathogens and consequently reduce the incidence of all infections, including RTIs in elderly subjects. Six weeks of treatment with RTB101 alone and in combination with everolimus met a prespecified endpoint of reducing the incidence of infections by 33% ($p=0.008$) and 38% ($p=0.001$), respectively, during a period of one year following initiation of therapy. We are evaluating RTB101 alone and in combination with everolimus in a Phase 2b clinical trial for the reduction in the incidence of RTIs in the elderly and expect to report top-line data from this trial in the second half of 2018. We expect market exclusivity for RTB101 alone and in combination with everolimus until at least 2031 in the United States, 2032 in major European markets, 2030 in Japan, and additional pending patent applications may prolong the exclusivity of these product candidates up to 2036.

Recent scientific findings, including those published in the scientific journals Cell, Nature and Science, suggest that aging and aging-related conditions, such as immunosenescence, are attributable not only to random cellular wear and tear, but also to specific intra-cellular signaling pathways, including the mTOR pathway. mTOR is a protein kinase that signals via two multiprotein complexes, known as TORC1 and TORC2. TORC1 inhibition has been observed to prolong lifespan, enhance immune function, ameliorate heart failure, enhance memory and mobility, decrease adiposity, and delay the onset of aging-related diseases in multiple animal studies. Specifically with respect to enhanced immune function, TORC1 inhibition was observed in preclinical studies to rejuvenate blood, or hematopoietic, stem cell function, increase infection-fighting white blood cell production and enhance antibody-mediated, or adaptive, immunity. On the other hand, TORC2 inhibition has been observed to decrease lifespan in preclinical studies and cause unwanted side effects of hyperlipidemia and hyperglycemia in certain animals and humans. Therefore, based on these observations and data from the Phase 2a clinical trial, we believe our TORC1 program is well-suited to improve immune function and counteract immunosenescence in the elderly.

The reduced ability of elderly patients to effectively detect and fight infections is most commonly manifested in their susceptibility to RTIs and the negative effects such infections have on their overall health. According to the U.S. Census Bureau, RTIs are the fifth leading cause of death in people age 85 and over and the seventh leading cause of death in people age 65 and over, and result in high healthcare burdens and costs for the elderly population and the healthcare system. The majority of RTIs are caused by viruses for which there are no approved therapies. Despite this, antibiotics, which are ineffective against viruses, are often prescribed indiscriminately to treat RTIs, which may cause side effects related to antibiotic use and contribute to the growing global problem of antibiotic resistance. As the elderly represent the fastest growing population in the world as a whole, we believe there is significant unmet medical need for innovative therapeutic options for reducing the incidence of RTIs by enhancing the function of the aging immune system.

We believe our approach to addressing RTIs in the elderly possesses several clinical and commercial advantages. Our TORC1 program offers an immunotherapy approach that has the potential to address a broad range of viral and bacterial pathogens. Statistically significant and clinically meaningful reductions in RTI incidence were observed in the Phase 2a clinical trial that evaluated RTB101 alone and in combination with everolimus. We believe the risk-to-benefit ratio of our program is well-suited to the elderly due to the following observations: our oral product candidates were well-tolerated in elderly subjects and were associated with no study drug-related serious adverse events in the Phase 2a clinical trial, and the doses being investigated in our ongoing Phase 2b clinical trial are 60 to 240 times lower than maximum tolerated doses established in prior clinical trials for other indications. Based on communications including those during a high-level policy meeting with the U.S. Food and Drug Administration, or FDA, to date, we believe a reduction in the incidence of RTIs has the potential to be a clinically relevant endpoint. Subject to receiving positive results from our ongoing Phase 2b clinical trial with respect to reduction in RTI incidence, we plan to conduct a Phase 3 pivotal program and to seek regulatory approval for commercialization of RTB101 alone or in combination with everolimus in the United States, Europe and Japan. In some markets, we may collaborate with third parties for the development and commercialization of our product candidates.

We were founded in 2016 by Chen Schor, who serves as our president and chief executive officer, Joan Mannick, M.D., who serves as our chief medical officer, and PureTech Health LLC, or PureTech Health, an affiliate of PureTech Health plc, an advanced clinical-stage biopharmaceutical company. Dr. Mannick led the TORC1 clinical program at Novartis Institutes for Biomedical Research Inc., or NIBR, prior to our in-licensing of the program. We were a subsidiary of PureTech Health until the closing of our Series B financing in November 2017. Based on the number of shares outstanding as of March 23, 2018, PureTech Health beneficially own shares representing approximately 34.9% of our outstanding common stock. In addition, PureTech Health has appointed two directors to our board of directors.

Our management team includes veterans in drug development and discovery, with executive experience in leading global pharmaceutical companies. We are supported by investors that include both private equity venture capital funds and public healthcare investment funds. Our investors include OrbiMed Advisors, Fidelity Management & Research Company, Rock Springs Capital, Quan Capital and Nest Bio.

Our Strategy

Our goal is to be a leading biopharmaceutical company focused on treating aging-related diseases. We strive to maintain a leadership position in the TORC1 inhibitor class of pharmaceutical products. The key elements of our strategy to achieve this goal include:

- *Rapidly advance our TORC1 program as immunotherapy for reducing the incidence of RTIs in elderly subjects.* We initiated our Phase 2b clinical trial of RTB101 alone and in combination with everolimus in elderly subjects at increased risk of mortality and morbidity due to RTIs in the second quarter of 2017, and we expect to report top-line data from this trial in the second half of 2018. If the results of our Phase 2b clinical trial are positive, we plan to initiate a Phase 3 clinical trial in 2019 with a goal to submit a new drug application, or NDA, to the FDA for regulatory approval of RTB101 alone or in combination with everolimus in the United States in 2020.

- *Develop our TORC1 program for additional indications.* We also intend to develop RTB101, alone or in combination with everolimus, for the treatment of additional aging-related diseases based on preclinical and clinical evidence on the effects of TORC1 inhibition. We believe that there is strong rationale to support the investigation of RTB101, alone or in combination with everolimus, for the treatment of additional aging-related indications, such as urinary tract infections, heart failure and neurodegenerative diseases.

- *Commercialize our product candidates in the United States and potentially collaborate with others globally to maximize their commercial value.* We plan to directly commercialize our product candidates in the United States with a sales force targeting top-prescribing physicians with high flow of elderly patients and may consider collaborating with third parties to broaden the distribution of our product candidates in the United States. In other markets for which commercialization may be less capital efficient for us, we may selectively pursue strategic collaborations with third parties in order to maximize the commercial potential of our product candidates. We believe there are significant opportunities to market RTB101, if approved, in Europe and Japan, which we may choose to pursue in collaboration with others.

- *Maintain and grow a robust intellectual property portfolio in the field of TORC1 inhibition for aging-related diseases.* We have an exclusive license to ten patent families directed to compositions of matter, methods and formulations covering RTB101 alone or in combination with everolimus. We intend to aggressively pursue and maintain broad intellectual property protection for RTB101 alone or in combination with everolimus or other compounds for the prevention of RTIs and the prevention or treatment of other aging-related diseases through U.S. and international patents.

- *Develop, acquire or in-license product candidates that enhance our global leadership position.* We have additional TORC1 inhibitor compounds in discovery that we may develop, and we may acquire or in-license other product candidates targeting TORC1 and other pathways that regulate aging to support our goal to be the leading biopharmaceutical company focused on the treatment of aging-related diseases with significant unmet medical need.

Our Product Pipeline

The following table summarizes key information about our product candidates.

* Other infections include those that the elderly are at increased risk of contracting, such as urinary tract infections.

** For heart failure with preserved ejection fraction, autophagy-related neurodegenerative diseases and certain other infections, we may be required to file an investigational new drug application, or IND, prior to initiating Phase 2 clinical trials. We expect to have the ability to initiate these Phase 2 clinical trials without the need to conduct prior Phase 1 clinical trials.

We also have a follow-on TORC1 inhibitor program at discovery stage.

Aging and its Regulation by the mTOR Pathway

Advances in the scientific understanding of aging have until recently been limited, despite high growth in the elderly population

The elderly are the fastest growing population around the globe. According to the U.S. Census Bureau, the population age 65 and older in the United States is expected to double by 2050 compared to 2012 estimates. According to global census data, there are nearly 150 million people age 65 and older, and approximately 20 million people age 85 years and older in the United States, the major European countries and Japan. Despite age being the major risk factor for multiple chronic diseases, we believe few therapies are being developed to target the aging immune system, and none have been approved.

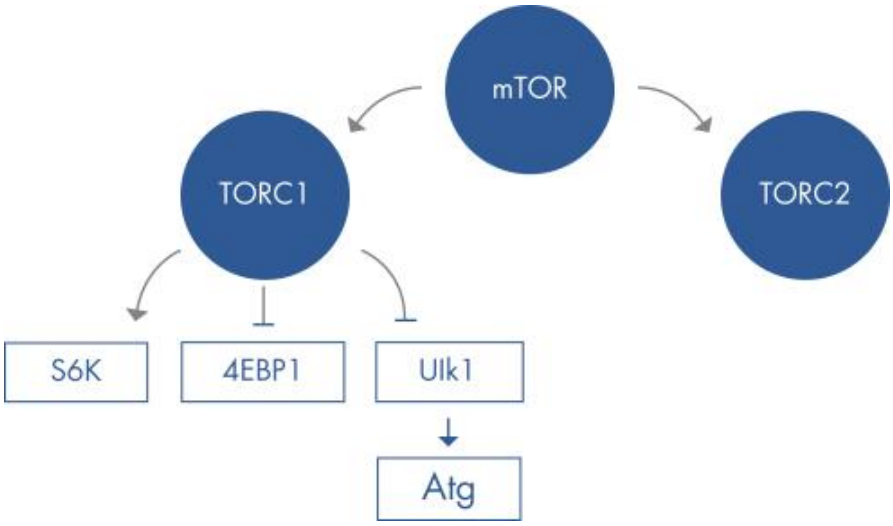
mTOR is an evolutionarily conserved pathway that regulates aging

mTOR is a serine/threonine protein kinase that regulates the process of aging and aging-related diseases and conditions. Inhibition of the mTOR pathway has been observed to prolong lifespan in multiple animals. These data support

the potential for drugs that target the mTOR pathway to have therapeutic benefits for aging and aging-related conditions in humans.

In preclinical studies, the mTOR pathway has been observed to be hyperactivated in some cell types, including hematopoietic stem cells, or HSCs, at an advanced age. It was observed that suppressing mTOR activity in these cell types to levels found at younger ages may enhance cell function, including their ability to generate white blood cells. Furthermore, preclinical studies found that mTOR activity stimulates protein synthesis and cell growth, but inhibits protective processes such as autophagy in which damaged proteins and organelles are broken down and recycled. Therefore, these studies suggest that increased mTOR activity is beneficial during years of growth and reproduction but may be harmful during post-reproductive years when cells accumulate damage and require protective mechanisms such as autophagy to prevent and repair damage.

mTOR signals via two multiprotein complexes, known as TORC1 and TORC2. TORC1 inhibition has been observed to prolong lifespan, enhance immune responses, ameliorate heart failure, ameliorate neurodegenerative diseases, enhance memory and mobility, decrease adiposity and delay onset of aging-related diseases in multiple animal studies. On the other hand, TORC2 inhibition has been observed to decrease lifespan and cause hyperlipidemia and hyperglycemia in certain animals and humans. Therefore, we believe the optimal approach for the treatment of aging-related conditions through mTOR inhibition is a regimen that inhibits TORC1 without inhibiting TORC2. mTOR within the TORC1 complex introduces phosphates to, or phosphorylates, multiple proteins including S6K, 4EBP1 and Ulk1, as shown in the figure below. More complete inhibition of TORC1, as measured by decreased phosphorylation of multiple proteins downstream of TORC1, may also be more beneficial compared to partial inhibition of TORC1 for the treatment of aging-related diseases.



We believe TORC1 inhibition may have therapeutic benefit in multiple aging-related diseases. Preclinical studies suggest that key mechanisms involved in the anti-aging effects of TORC1 inhibition include improved stem cell function, increased autophagy, increased expression of mitochondrial proteins that are important for energy production and increased expression of proteins that are responsible for cellular maintenance and repair. Based on preclinical data, these biological effects have the potential to improve multiple aging-related pathologies:

1. *Decreased immune function and increased risk of infections.* The immune system has several important functions, including protection against harmful pathogens, cancer immunosurveillance and clearance of senescent cells. Innate immunity is the body's first line of defense against a wide range of pathogens, while adaptive immunity is a more pathogen-specific immune response that develops over time. Immune cells are produced by HSCs in the bone marrow, which can lose functionality with age. In preclinical studies, aged dendritic cells, a type of innate immune cell, demonstrated defective Type 1 interferon production, a central component of anti-viral immunity, in response to a virus. This response is consistent with the observation that dendritic cells from older subjects produced less interferon upon stimulation with a virus than those from younger subjects. Adaptive immunity also declines with age. The number and functionality of certain white blood cells known as lymphocytes, including antibody-producing B lymphocytes, have been observed to be

decreased in elderly human subjects. We believe that this decline in immune function contributes to the higher incidence of common infections such as respiratory and urinary tract infections in the elderly.

2. *Decreased mitochondrial function and organ dysfunction.* During aging, mitochondrial function, which is important for metabolism and energy production in cells, is diminished. This diminution is linked to a switch from more efficient fatty acid oxidation to less efficient glucose oxidation in aging organs. The detrimental nature of this metabolic change has been extensively described in animal and human studies of aging-related conditions, including heart failure.

3. *Decreased autophagy and accumulation of damaged proteins*. Autophagy is the process in which a cell breaks down and recycles damaged cellular components, including damaged and aggregated proteins. Preclinical data suggests that an aging-associated decrease in autophagy leads to the accumulation of toxic proteins and may result in aging-associated pathologies such as neurodegeneration.

Immunosenescence and Respiratory Tract Infections in the Elderly

Potential for TORC1 inhibition to address decreased immune function associated with aging

TORC1 inhibition has been observed to enhance immune function in at least three independent preclinical studies to date, conducted by laboratories at the University of Michigan, Emory University and St. Jude Children's Research Hospital, where administration of mTOR inhibitors improved immune response to influenza vaccination. Further, findings from these preclinical studies suggest that short-term treatment of aged animals with a TORC1 inhibitor can rejuvenate HSC function, increase the number of infection-fighting white blood cells, and increase longevity. We believe these findings suggest that TORC1 inhibition has the potential to improve immune function in elderly humans.

Respiratory tract infections in the elderly

The reduced ability of the aging immune system to effectively detect and fight infections results in increased susceptibility of the elderly to RTIs, which, in turn negatively impacts such patients' overall health and quality of life. We believe that decreasing the incidence of RTIs is a large unmet medical need in the elderly, particularly in subjects at an increased risk of RTI-related morbidity and mortality. We believe there is a significant unmet medical need for an innovative therapy to reduce the incidence of RTIs in the elderly for the following reasons:

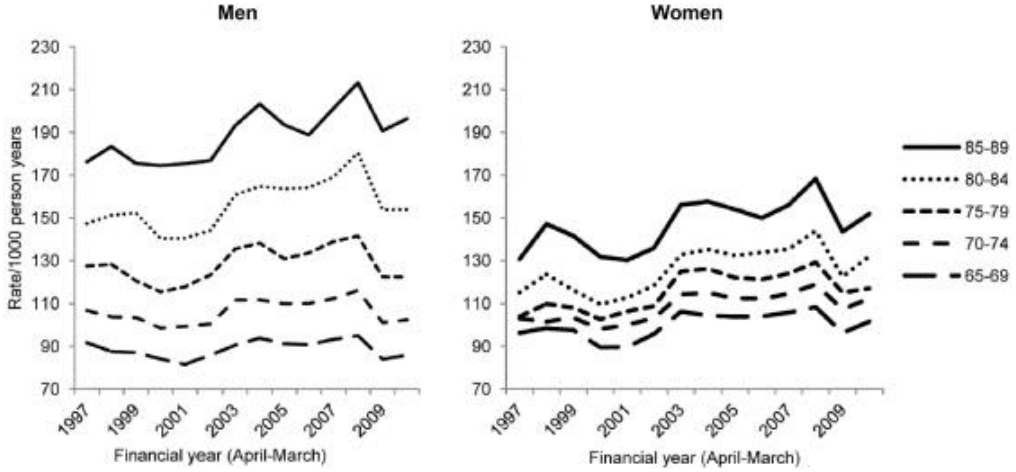
- *The large and growing elderly population is particularly susceptible to morbidity and mortality from RTIs*. The elderly represent the fastest growing population across the globe. In the United States, RTIs are the fifth leading cause of death in people age 85 and over and the seventh leading cause of death in people age 65 and over. Mortality among people age 75 and over is highest each year during winter cold and flu season. Age is a risk factor for RTIs, with men aged 85-89 experiencing lower RTIs at twice the rate of men aged 65-69. As a result, RTIs, which are typically not serious in healthy adults, are exacerbated in the elderly. Elderly patients with comorbidities may also be at a higher risk of morbidity and mortality due to RTIs as compared to healthy elderly subjects. Comorbidities among the elderly aged 65 and older are common, with approximately 14% having chronic obstructive pulmonary disease, or COPD, 7% having asthma, 20% having type 2 diabetes mellitus, or T2DM, and 13% having congestive heart failure, or CHF. Prior to initiating the Phase 2b clinical trial, PureTech Health conducted market research with five payers and 55 physicians in the United States. The results of the research provided further support that the efficacy demonstrated in the Phase 2a clinical trial is clinically meaningful and that there is unmet medical need in the elderly, particularly in the elderly at high risk of mortality from RTIs. Specifically, a reduction in the incidence of RTIs of similar or lower magnitude to that observed in the Phase 2a trial was described as a clinically meaningful improvement by the majority of respondents in a survey of 50 physicians. Further, 84% of the physicians who participated in the survey perceived that there is unmet need for either prophylactics or treatment options, or both, for viral respiratory infections. Phone interviews with payers also illustrated that, subject to FDA approval, payers may be able to include a product with our efficacy and safety profile into a preferred tier on their formularies and may request a modest rebate. The following figures highlight the number of elderly people in the United States, major European countries and Japan, along with their comorbidities, based on global census data and our market research performed in the U.S., and the historical rates of lower RTIs in the elderly population in the U.K.

Estimated Size of Population Susceptible to RTI-related Morbidity and Mortality

	U.S.	EU5	JP
Elderly people (65-74 years old): *With comorbidities (COPD, asthma, T2DM, CHF)*	11M	13M	7M
Elderly people (75-84 years old): *With comorbidities (COPD, asthma, T2DM, CHF)*	7M	11M	6M
Elderly people (85+ years old):	6M	9M	5M
# Elderly people (2016)	**24M**	**33M**	**18M**
Average Annual Growth Rate	3%	2%	1%

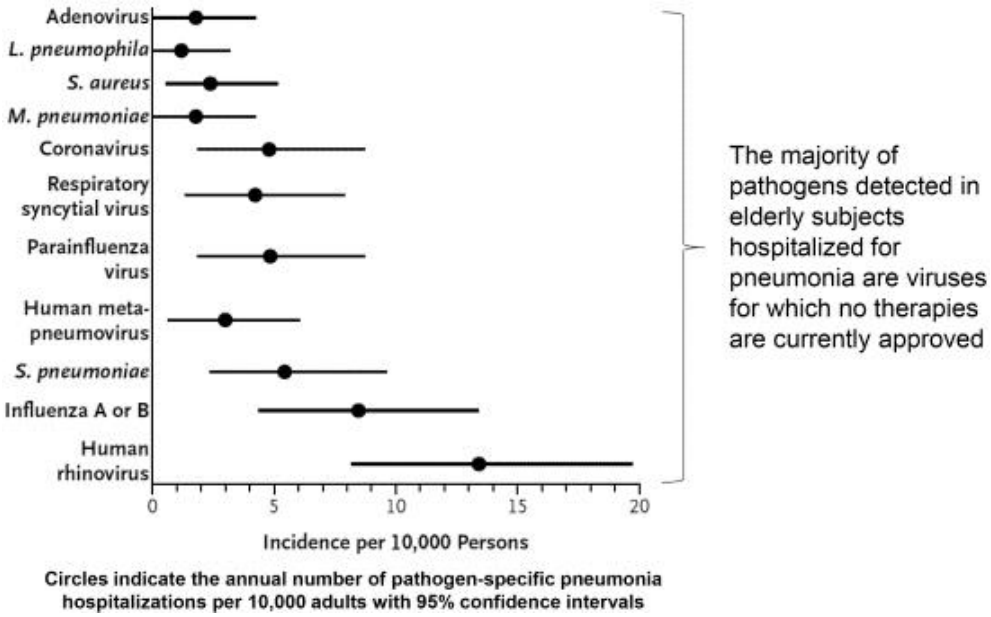
An estimated 75 million elderly people in 2016 were at increased risk of RTI-related morbidity and mortality in U.S., the major European countries and Japan

Lower Respiratory Tract Infection Rates Increase with Age



- *RTIs contribute to high healthcare burden and costs*. At least 11%, 56% and 80% of CHF exacerbations, COPD exacerbations requiring hospitalization and asthma exacerbations, respectively, are associated with RTIs, and 7% of people aged 85 years and over go to the emergency room with RTIs each year. In addition, two-thirds of people aged 85 and over who go to the emergency room for infection-related reasons are hospitalized, and once hospitalized, one-third of people aged 85 and over are admitted to a nursing home. These figures illustrate the large economic impact of RTIs on the healthcare system in the United States.

- *The majority of RTIs are caused by viruses for which no available therapy exists*. The majority of RTIs are caused by viruses, most of which lack approved prophylactics or therapies, leaving physicians with few treatment options. Based on Center for Disease Control, or CDC, guidelines, vaccines are given to prevent influenza and pneumococcal infections. However, even if vaccinated, the elderly are less likely to develop sufficient protective immunity against influenza and pneumococcal infections due to immunosenescence. In addition, vaccines against most of the viral pathogens that cause RTIs are not currently available. The following figure illustrates the specific pathogens detected in patients 80 years or older hospitalized with community-acquired pneumonia.



- *Antibiotics are often prescribed indiscriminately to treat RTIs, leading to potential side effects and contributing to growing antibiotic resistance*. Antibiotics, which are ineffective against viruses, are often prescribed indiscriminately to treat RTIs, which may cause side effects related to antibiotic use and contribute to the growing global problem of antibiotic resistance. As antibiotic use is a primary driver of antibiotic resistance, we believe that reducing the incidence of RTIs in the elderly could also indirectly limit the rise of antibiotic-resistant bacteria. Furthermore, the elderly are at increased risk of antibiotic-related adverse events due to increased organ sensitivity, increased exposure due to changes in pharmacokinetics, and polypharmacy. According to a study conducted by McGill University, antibiotics have been linked to 17% of adverse drug-related events in the elderly who visit emergency departments. Antibiotic use can also lead to lethal superinfections such as *C. difficile* infections.

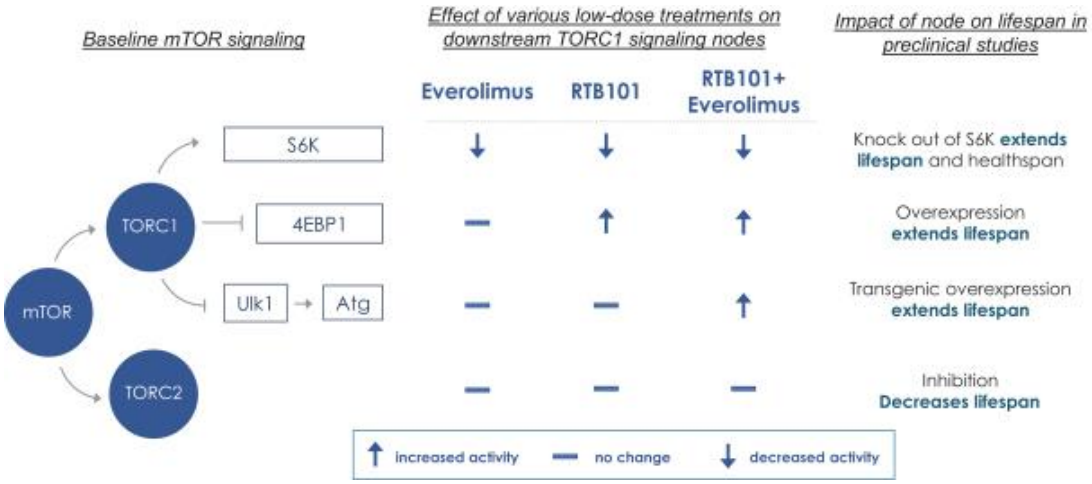
- *Lack of immunotherapy drugs to address RTIs*. Immunotherapies ideally enhance both innate and adaptive immunity to provide broad, acute and long-lasting protection against pathogens. Currently, however, there are no approved immunotherapies to enhance either innate or adaptive immunity in the elderly. We believe RTB101 alone or in combination with everolimus represent immunotherapies aimed at enhancing either innate or innate and adaptive immunity in the elderly, and thereby decreasing the incidence of RTIs caused by a broad spectrum of pathogens, particularly viral pathogens. In addition, beyond an individual level, we believe immunotherapies may benefit the wider population through indirect protection that occurs when a large percentage of the population has become immune to a disease, thereby preventing or limiting the spread of infection and providing a measure of protection for individuals who are not immune, a phenomenon known as herd immunity.

Our TORC1 Program

Overview

In March 2017, we obtained a license from Novartis to the worldwide rights to RTB101 for all indications, and the rights to use everolimus in combination with RTB101 for all aging-related indications. RTB101 is an orally administered, small molecule, potent TORC1 inhibitor that binds to the active site of mTOR on the TORC1 complex, a mechanism known as catalytic inhibition. In contrast, everolimus, also an orally administered small molecule, inhibits mTOR activity by changing the shape of TORC1, a mechanism known as allosteric inhibition, that is distinct from and synergistic with catalytic inhibition.

The downstream signaling cascade of TORC1 that we believe occurs in scenarios of baseline, RTB101 alone and RTB101 in combination with everolimus are pictured in the following figure.



Our TORC1 program includes evaluation of RTB101 alone because we believe RTB101 monotherapy can effectively inhibit phosphorylation of multiple downstream signaling nodes of TORC1, specifically S6K and 4EBP1, that are key drivers of TORC1 downstream activity. Decreased phosphorylation of S6K leads to decreased activity, while decreased phosphorylation of 4EBP1 and Ulk1 leads to increased activity. We believe RTB101 alone consistently inhibits more downstream signaling nodes of TORC1 than a rapalog, such as everolimus, alone. Furthermore, we believe RTB101 at the low doses that we are evaluating in our clinical studies can achieve these effects without inhibiting TORC2. RTB101 at higher doses, while able to more completely inhibit TORC1, may also inhibit TORC2, which may lead to undesirable side effects.

Our TORC1 program also includes evaluation of RTB101 in combination with everolimus, as the combination of catalytic and allosteric inhibitors may yield complete inhibition of all nodes downstream of TORC1, including 4EBP1 and Ulk1, without affecting TORC2. It was observed in preclinical in vitro studies that RTB101 and everolimus at the comparable doses that we are evaluating in our clinical trials synergistically inhibit 4EBP1. The synergy of RTB101 and everolimus, as measured by Loewe additivity, was up to 43% in those studies. Loewe additivity in excess of 30% is considered to be high. We believe everolimus may induce a conformation change in TORC1 that allows lower concentrations of RTB101 to inhibit TORC1 without inhibiting TORC2. Preclinical and clinical data suggest that for some indications, RTB101 monotherapy may be adequate to yield clinically meaningful benefit to patients, while for other indications, the combination of RTB101 and everolimus may be more beneficial. Accordingly, our TORC1 program includes evaluation of both RTB101 alone and in combination with everolimus.

Clinical Development of RTB101 Alone and in Combination with Everolimus

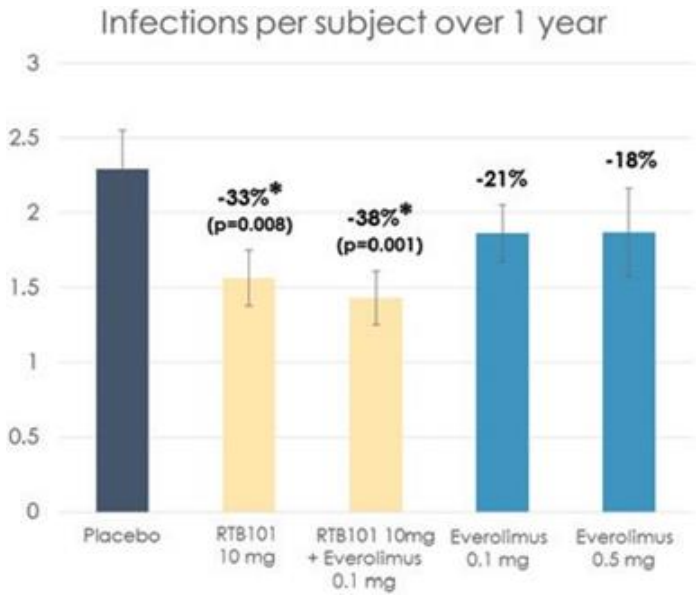
We consider data from a Phase 2a clinical trial conducted by our licensor, Novartis, which became available in 2016 to be the most directly relevant dataset for our near-term development of RTB101 alone and in combination with everolimus, including the design of our ongoing Phase 2b trial evaluating the safety, tolerability and efficacy of our product candidates to reduce the incidence of RTIs in the elderly. If results from our ongoing Phase 2b clinical trial are positive, we intend to initiate a Phase 3 program for RTB101 alone or in combination with everolimus in 2019. We believe that preclinical and clinical safety data of high-dose RTB101 alone and in combination with everolimus, at similar or higher does than those tested in our Phase 2b clinical trial, that was generated by our licensor, Novartis, in clinical trials conducted from 2006 to 2016 provide additional support for the clinical development of our program. The potential for TORC1 inhibition to ameliorate immunosenescence was also demonstrated in a previous Phase 2a clinical trial of everolimus monotherapy conducted by Novartis and published in Science Translational Medicine in December 2014.

Phase 2a Clinical Development

The primary objectives of the RTB101 and RTB101+everolimus Phase 2a clinical trial were to assess the safety, tolerability and efficacy of RTB101 alone and in combination with everolimus compared to placebo in enhancing the immune response to vaccination in elderly subjects, as determined by the subjects' immune response to the seasonal influenza vaccine. A pre-specified exploratory endpoint assessed the effect of a six-week course of RTB101 alone or in combination with everolimus on infection rates during the year following initiation of study drug treatment. The trial was a double-blinded, placebo-controlled, randomized clinical trial that enrolled a total of 264 male and female subjects at least 65 years of age without underlying unstable medical conditions, and was conducted across 12 trial centers in the southern hemisphere. Subjects were randomized to one of five treatment arms, in which they were administered daily oral doses of everolimus 0.1 mg, everolimus 0.5 mg, RTB101 10 mg, RTB101 10 mg+everolimus 0.1 mg, or placebo. The trial met its primary endpoint and the pre-specified exploratory infection rate endpoint.

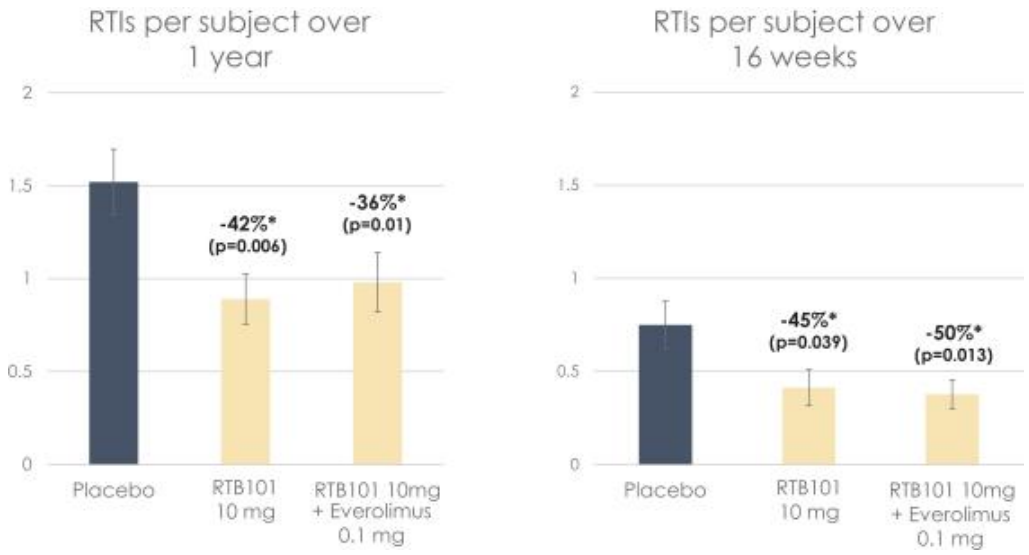
Subjects were treated for six weeks with the study drug and, after a two week drug-free interval, were given the seasonal influenza vaccine. The subjects were followed for one year following initiation of study drug treatment. The overall infection rate in each treatment group was assessed by having subjects record any infections they experienced during the year following the initiation of study drug treatment in a diary. The sites reviewed the infection diary at each study visit. In addition, sites administered infection questionnaires during phone calls with subjects that occurred weekly during the six-week study drug dosing period and then monthly for the remainder of the trial. Investigators reviewed and approved the information contained in the telephone questionnaire reports within 24 hours. The infection data in the diaries and telephone reports were reconciled by sites prior to entering infections in the clinical trial database.

In the RTB101 monotherapy and RTB101+everolimus combination treatment arms in the intent-to-treat population, statistically significant and clinically meaningful reductions in the annual rate of infections of 33% (p=0.008) and 38% (p=0.001), respectively, compared to placebo, were observed. The FDA utilizes the reported statistical measures when evaluating the results of a clinical trial, including statistical significance as measured by p-values as an evidentiary standard of efficacy, to evaluate the reported evidence of a product candidate's safety and efficacy. If not otherwise specified, we used a conventional 5% or lower p-value ($p<0.05$) to define statistical significance for the clinical trials and data presented in this Annual Report on Form 10-K. A lesser, non-statistically significant effect was observed with everolimus monotherapy.

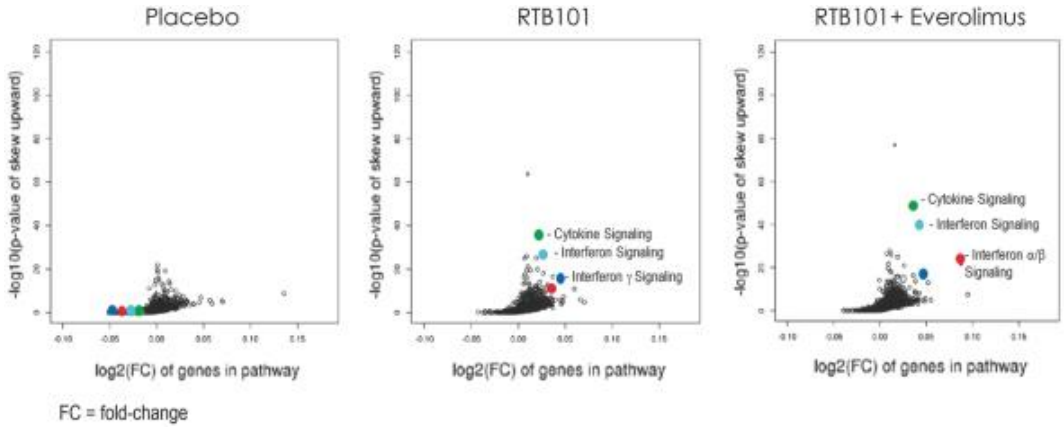


Since the most common infections that occurred during the trial were RTIs, a post-hoc analysis was performed to determine whether a reduction in RTIs contributed to the significant reduction in infections at one year following initiation of study drug treatment in the RTB101 monotherapy and RTB101+everolimus combination treatment arms. As shown in the figure below, both RTB101 monotherapy and the RTB101+everolimus combination therapy were observed to reduce the incidence of RTIs at one year by 42% (p=0.006) and 36% (p=0.01), respectively, in the intent-to-treat population. Greater reductions in the incidence of RTIs were observed during the six-week dosing period in the RTB101 monotherapy and

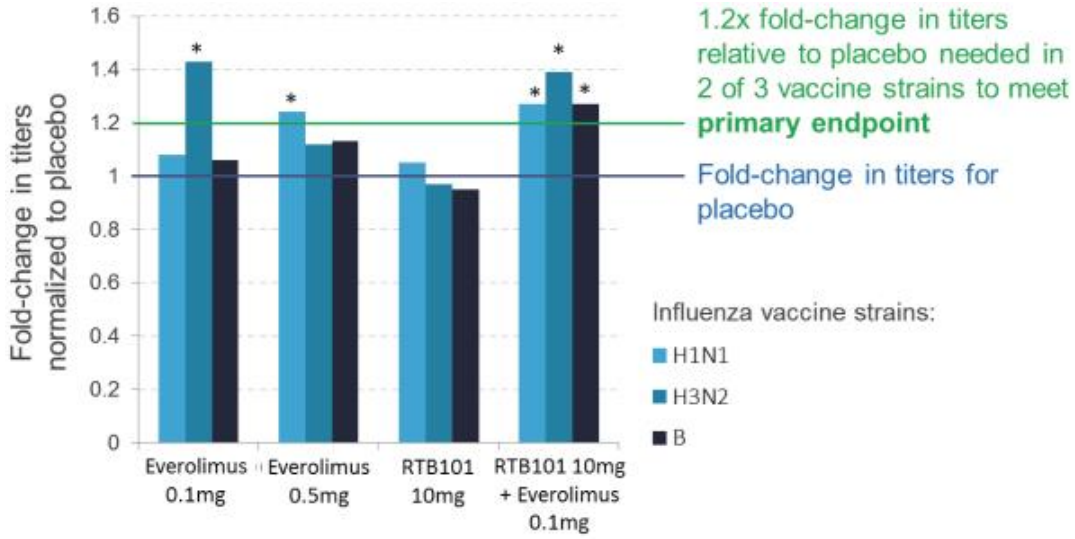
RTB101+everolimus combination arms. Given that the magnitude of the reduction in RTI incidence was greater at six weeks than at one year, these findings suggest that the reduction in RTI rates was greatest during the period when subjects were receiving the study drug. The typical duration of the peak cold and flu season is approximately 16 weeks. As shown in the figure below, analysis of the Phase 2a clinical data also revealed reductions of 45% (p=0.039) and 50% (p=0.013) in RTIs from treatment with RTB101 alone and in combination with everolimus, respectively, during the 16 weeks following initiation of therapy despite only six weeks of treatment.



To assess possible molecular mechanisms underlying the decrease in infection rates in the RTB101 monotherapy and RTB101+everolimus combination treatment groups, mRNA sequencing analysis of whole blood from subjects at baseline and after six weeks of study drug treatment was conducted. Analysis of whole-blood gene expression data revealed a highly statistically significant up-regulation of pathways related to interferon signaling in the RTB101 monotherapy and RTB101+everolimus combination treatment arms but not in the placebo arm, as shown in the figures below. Genes that were up-regulated the most, including MX1, OAS3, ISG15 and IFIT1, encode a subset of Type 1 interferon-induced proteins that play a critical role in the acute, innate immune response to viruses, suggesting that RTB101 alone and in combination with everolimus may enhance innate immunity. Pathways, or groups of genes, related to cytokine signaling and interferon signaling were significantly upregulated, with p-values ranging between 10^{-45} to 10^{-10}.



While the effects of RTB101 monotherapy and RTB101+everolimus combination therapy on reducing RTIs incidence in the elderly and up-regulating innate immunity genes were comparable, only the combination therapy met the primary endpoint of the Phase 2a clinical trial of enhancing influenza vaccination response, defined as a greater than 20% increase in antibody concentrations, or titers, to at least two of the three tested influenza vaccine strains as compared to placebo, measured at 12 weeks following initial dosing of the study drug. We believe these results suggest that the RTB101+everolimus combination therapy may also enhance the adaptive immune system, in addition to enhancing the innate immune system, given that the RTB101+everolimus combination resulted in broader TORC1 inhibition. The adaptive immune response to influenza vaccination across all treatment arms is shown in the figure below, where asterisks indicate a 100% probability that titers are greater than those observed in the placebo group.



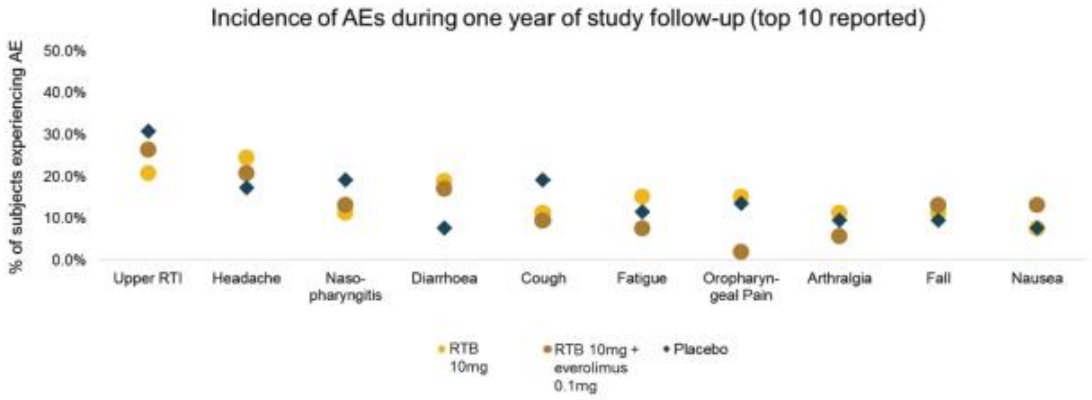
Overall, all treatment regimens were well tolerated. None of the participants in the active treatment arms experienced a serious adverse event, or SAE, that was related to the study drug. The following table summarizes the SAEs experienced by trial subjects during the year they were followed in the trial.

	Everolimus 0.1mg	Everolimus 0.5mg	RTB101 10mg	RTB101 10mg + Everolimus 0.1mg	Placebo
Total SAEs	4	9	9	6	8
Subjects with SAEs	3	8	6	3	5
% of subjects with SAEs*	5.8	14.8	11.3	5.7	9.6

* Percentages are based on the total number of subjects in each arm that received at least part of one dose of study drug

The ten most prevalent adverse events, or AEs, during the 12 months that patients were followed in the trial is summarized in the figure below. Diarrhea was the most frequently reported AE that occurred more often in the study drug treatment groups than the placebo groups and was generally mild or moderate in severity, transient and resolved with no treatment. Of note, the rate of upper RTI, nasopharyngitis and cough was lower for RTB101 monotherapy and RTB101+everolimus combination than for placebo, suggesting greater freedom from respiratory symptoms in the treatment groups as compared to the placebo groups. Furthermore, rates of hyperglycemia and hypercholesterolemia, which are AEs associated with TORC2 inhibition, were less than 5% in all treatment groups and were the same or lower in the mTOR

inhibitor treatment groups than the placebo groups, suggesting that these low dose mTOR inhibitor treatment regimens did not inhibit TORC2.



We believe that the Phase 2a clinical trial results provide proof of concept for the potential therapeutic benefit of RTB101 alone or in combination with everolimus as immunotherapy to reduce the incidence of RTIs in elderly patients, given the statistically significant and clinically meaningful reduction in RTI rates, the increased expression of innate anti-viral genes and the enhanced immune response to vaccination observed across the treatment groups.

Ongoing Phase 2b Clinical Development

We are conducting a randomized, double-blinded, placebo-controlled Phase 2b clinical trial to assess the safety, tolerability and efficacy of 16 weeks of treatment with RTB101 alone or in combination with everolimus as compared to placebo in elderly patients without unstable medical conditions but who are at increased risk of RTI-related morbidity or mortality. Elderly patients at increased risk of RTI-associated morbidity and mortality are defined as subjects who are 85 years of age or older or subjects 65 years of age or older with asthma, chronic obstructive pulmonary disease, chronic bronchitis, Type 2 diabetes mellitus, congestive heart failure, an emergency room visit or hospitalization for an RTI within the past 12 months, or who are current smokers. We are conducting the trial in two parts across two hemispheres. The first part was conducted during the winter cold and flu season in the southern hemisphere. Following an interim analysis that we conducted in October 2017, we commenced the second part of the study, which was initiated during the winter cold and flu season in the United States in the fourth quarter of 2017. We expect to report top-line data from this trial in the second half of 2018. The primary endpoint of the trial is to determine if RTB101 alone or in combination with everolimus decreases the percentage of subjects with RTIs compared to placebo during the 16-week administration period.

In the first part of the trial, 179 patients were randomized to receive RTB101 10 mg daily, RTB101 5 mg daily or placebo daily. We selected RTB101 10 mg daily as a dose because in the Phase 2a clinical trial, the same dose was well-tolerated and was observed to significantly decrease the rate of all infections as well as the rate of RTIs, and was associated with upregulation of antiviral gene expression in whole blood. To determine the minimal efficacious dose of RTB101, we also evaluated RTB101 5 mg daily in the Phase 2b trial.

An interim analysis on data from the first part of the trial was completed in October 2017 by an independent data monitoring committee, or DMC. The DMC reviewed the safety and efficacy data from the first part of the trial and selected the doses of RTB101 and RTB101 in combination with everolimus to be tested in the second part of the trial in the United States.

We commenced the second part of the Phase 2b clinical trial in the fourth quarter of 2017. Based on the DMC recommendation, we expect to randomize at least 424 patients to receive placebo or one or more of the following TORC1 inhibitor treatment regimens: RTB101 10 mg once daily, RTB101 10 mg twice daily and RTB101 10 mg in combination with everolimus 0.1 mg.

We are studying the combination of RTB101 and everolimus 0.1mg because in the Phase 2a clinical trial, this combination not only reduced the incidence of infections similar to RTB101 monotherapy, but also led to a greater improvement in influenza vaccination response than either RTB101 or everolimus monotherapy.

The Phase 2b clinical trial was designed to have a greater than 80% power to detect a statistically significant reduction in the percentage of subjects with RTIs, assuming an effect size of 40% reduction. The effect size of 40% was conservatively estimated based on the reduction observed in the Phase 2a RTI rates at 16 weeks, which is the duration specified for the Phase 2b primary endpoint, of 45% (p=0.039) and 50% (p=0.013) in the RTB101 monotherapy and RTB101+everolimus combination arms respectively.

Based on communications with the FDA, including those during a high-level policy meeting, to date, we believe a reduction in the incidence of RTIs has the potential to be a clinically relevant endpoint. We completed a pre-investigational new drug, or pre-IND meeting, with the FDA in July 2017 and subsequently submitted an investigational new drug application, or IND, for RTB101 alone and in combination with everolimus as immunotherapy designed to reduce the incidence of RTIs in elderly patients at increased risk of RTI-related morbidity or mortality.

Phase 3 Clinical Development Plan

If the results from the ongoing Phase 2b clinical trial are positive, we intend to conduct two Phase 3 pivotal clinical trials across two hemispheres. The Phase 3 clinical program is expected to start in the southern hemisphere in the first half of 2019 at the beginning of the winter cold and flu season and run through the second quarter of 2020. If our Phase 3 clinical trials are successful, we anticipate filing an NDA with the FDA in 2020, and an MAA with the EMA in 2021.

If the results from the ongoing Phase 2b clinical trial are favorable for RTB101 monotherapy, we expect to randomize approximately 600 elderly subjects at increased risk of RTI-associated morbidity and mortality to receive daily oral administration of RTB101 monotherapy or placebo for 16 weeks in each of the proposed Phase 3 clinical trials. The primary endpoint would be the reduction in RTI incidence over the dosing period.

If the results from the ongoing Phase 2b are not positive for RTB101 monotherapy but are positive for the RTB101+everolimus combination therapy, we expect to initiate a Phase 3 program with the combination of RTB101+everolimus and may include enhanced immune response to vaccination as an additional co-primary endpoint. In connection with our development plan for RTIs, we may consider and initiate certain clinical studies to explore biomarker changes.

Safety Data from Clinical and Preclinical Development at High Doses of RTB101 Alone and in Combination with Everolimus

Originally, RTB101 was developed for oncology indications. In preclinical studies, at doses higher than those we are developing, RTB101 was found to prevent cellular proliferation and tumor progression. Clinical trials in humans were conducted under two open INDs for RTB101 filed with the FDA Division of Oncology Products. More than 440 oncology patients have been treated with RTB101 alone in doses up to 1,600 mg per day, or in combination with other drugs including 200 mg of RTB101 in combination with 2.5 mg of everolimus per day. RTB101 has also been administered to more than 60 healthy volunteers in pharmacokinetic, or PK, studies at doses of up to 1,000 mg per day. To date, the majority of the reported adverse events, or AEs, were mild or moderate and include gastrointestinal disturbances, fatigue, decreased appetite, rash and thrombocytopenia, which are consistent with those that have been reported for marketed mTOR inhibitors such as rapamycin and everolimus. No dose-limiting toxicities occurred at doses less than 800 mg per day, and the maximum tolerated dose for RTB101 as a monotherapy was established at 1,200 mg per day. We are developing RTB101 at daily doses of 5 mg to 20 mg, 60 to 240 times lower than the established maximum tolerated dose, and therefore expect the RTB101 to have an acceptable tolerability profile for the indications that we plan to pursue.

Standard preclinical safety and good laboratory practice, or GLP, toxicology studies, up to six months in rats and dogs, have been completed for RTB101, which we believe support the clinical development of the program.

Other Potential Indications for Our TORC1 Program

We may evaluate RTB101 alone or in combination with everolimus or other drugs for the treatment of additional indications, such as heart failure with preserved ejection fraction, urinary tract infections, Huntington’s disease, Parkinson’s disease and Amyotrophic Lateral Sclerosis. We plan to initiate at least one Phase 2 proof of concept study in 2018. We expect to select indications based on strong scientific rationale, preclinical or clinical data, unmet medical need and other relevant considerations.

Prevention of recurrent urinary tract infections

Urinary tract infections, or UTIs, are the most common bacterial infection in the elderly, with the incidence higher in women than men. According to studies of 959 and 395 women published in 2000 and 2010, respectively, nearly 10% of women older than 65 years of age and nearly 30% of women over the age of 85 reported having a UTI within the 12—month period preceding the study. The incidence of UTIs also increases substantially in men over the age of 85 years. Elderly subjects who have had a prior UTI are at increased risk of a recurrent UTI. Urinary tract infections are most commonly bacterial, and E. coli is the organism most frequently responsible for UTIs. Hence, empiric treatment of UTIs with antibiotics is common, and UTIs are the most common reason for antibiotic prescriptions in older adults.

In the Phase 2a clinical trial, a decrease in the rate of UTIs was observed in the RTB101 10 mg monotherapy and RTB101 10 mg+everolimus 0.1 mg combination arms as compared to placebo. We believe these data suggest that RTB101 alone or in combination with everolimus may have therapeutic benefit for reducing the rate of UTIs in the elderly, particularly elderly at risk for recurrent UTIs.

Treatment of viral respiratory tract infections

In the Phase 2a clinical trial, an increase of antiviral gene expression was observed in the RTB101 10 mg monotherapy and RTB101 10 mg+everolimus 0.1 mg combination arms. We plan to conduct a biomarker study to assess the speed at which antiviral genes are upregulated after elderly subjects are treated with RTB101 alone or in combination with everolimus. If we observe a rapid increase of antiviral gene expression, we believe RTB101 alone or in combination with everolimus may have therapeutic benefit for the treatment of viral RTIs.

Heart failure with preserved ejection fraction

Heart failure is one of the most common causes of hospitalizations in people age 65 and older, and heart failure with preserved ejection fraction, or HFpEF, affects about 2.25 million people in the United States, and a combined 6.24 million in the United States, Europe and Japan. HFpEF predominantly affects elderly subjects, particularly older women, in whom 90% of new heart failure cases are HFpEF. Patients with HFpEF experience the clinical symptoms of heart failure, despite having the percentage of total blood in the left ventricle of the heart that is pushed out with each heartbeat, known as ejection fractions, in the normal range. These symptoms are attributable in part to stiffened heart muscle that limits blood flow into the heart, known as diastolic dysfunction. Outcomes following hospitalization for decompensated HFpEF are poor. Approximately one third of patients are rehospitalized or die within 90 days of discharge. To date, there are no FDA approved therapies to reduce hospitalization or mortality for HFpEF.

According to scientific literature published by research groups at the Harvard Stem Cell Institute and the University of Washington, aging mice develop stiffened heart muscle and diastolic dysfunction similar to elderly humans with HFpEF. Preclinical studies have shown that a 10 week course of mTOR inhibitor therapy reverses diastolic dysfunction in aging mice. This beneficial effect is likely partly due to an increase in proteins involved in mitochondrial function and fatty acid oxidation. Fatty acids are the predominant substrate used in mitochondrial energy production in healthy adults, but are replaced by glucose as the preferred substrate in heart failure. The shift to glucose as a substrate results in less ATP production by mitochondria. Since ATP is the main cellular fuel, a decrease in ATP production may contribute to heart failure. mTOR inhibitors shift mitochondria back to using fatty acids as a substrate and as a result may increase ATP production in the heart and improve heart function. These findings suggest that RTB101 alone or in combination with everolimus may have therapeutic benefit for the treatment of HFpEF in humans.

Huntington’s disease

Huntington’s disease, or HD, is a disease that affects neurons in the brain and causes movement, psychiatric and cognitive impairment. HD is caused by mutations in a gene encoding protein called huntingtin. Mutant huntingtin forms aggregate in neurons and cause the neurons to degenerate. The mutant huntingtin aggregates can be cleared from neurons by a process called autophagy in which cells remove and recycle intracellular debris including protein aggregates. Preclinical data from brain slices in a HD mouse model has shown that RTB101 in combination with everolimus synergize to prevent neurodegeneration, likely by inducing autophagy and clearing mutant huntingtin aggregates. We believe these findings support the potential that RTB101 in combination with everolimus to have therapeutic benefit for the treatment of HD.

Parkinson's disease

Parkinson's disease, or PD, is a progressive neurodegenerative disease that affects approximately 7.5 million people worldwide. The incidence of PD increases rapidly in people 60 years of age and older, with a mean age at diagnosis of 70.5 years. Patients with PD develop shaking, rigidity, slowness of movement and difficulty walking. Similar to HD, PD may be attributed in part to neuronal damage caused by the accumulation within neurons of abnormal aggregates containing the protein a-synuclein. Preclinical studies in mouse models of PD have shown that mTOR inhibition can induce autophagy, reduce a-synuclein accumulation and decrease neuronal cell death. Therefore, induction of autophagy with RTB101 in combination with everolimus may have therapeutic benefit for patients with PD.

Amyotrophic Lateral Sclerosis

Amyotrophic Lateral Sclerosis, or ALS, is a fatal, age-related neurodegenerative disorder characterized by progressive loss of both upper and lower motor neurons in the brain and spinal cord. ALS is the most common motor neuron disorder and is estimated to affect 12,000-30,000 people in the U.S. The median age of onset of ALS is 64 years, and is characterized by diseased muscle atrophy, spasticity and quadriplegia, culminating in death within 3–5 years of disease onset due to respiratory failure. Genetic studies of ALS patients have identified mutations in autophagy pathway genes including *p62/SQSTM1*, *OPTN*, *TBK1*, *VCP*, and *C9ORF72*. Further, enhancing autophagy has shown benefit in multiple preclinical models of ALS, hence we believe that induction of autophagy with RTB101 in combination with everolimus may have therapeutic benefit for patients with ALS.

Intellectual Property

We strive to protect the proprietary technologies that we believe are important to our business, including seeking and maintaining patent protection intended to cover the composition of matter of our product candidates, including RTB101, their methods of use, related technology, and other inventions that are important to our business. We licensed a patent portfolio of ten patent families from Novartis. See "—License Agreement with Novartis." As of March 23, 2018, one family within this patent portfolio covering compositions of matter was issued in 42 countries and is pending in five. This patent family is expected to expire in 2026 before patent term extensions. We expect market exclusivity for RTB101, alone and in combination with everolimus, until at least 2031 in the United States, 2032 in major European markets, and 2030 in Japan, and additional pending patent applications covering methods of enhancing immunity, reducing incidence of RTIs and other infections, and other indications, may prolong the exclusivity of these product candidates up to 2036. In October 2017, we filed an additional patent application directed to compositions of matter for novel mTOR inhibitors.

In addition to patent protection, we rely on trade secrets and confidentiality agreements to protect our technology, know-how and other aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

Our success will depend significantly on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions, and know-how related to our business, defend and enforce the patents we own or control, maintain our licenses to use intellectual property owned by third parties, preserve the confidentiality of our trade secrets, and operate without infringing the valid and enforceable patents and other proprietary rights of third parties.

The patent positions of biopharmaceutical companies like us are generally uncertain and involve complex legal, scientific and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Consequently, we do not know whether any of our product candidates will be protectable or remain protected by enforceable patents. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient proprietary protection from competitors. Any patents that we hold or control may be challenged, circumvented or invalidated by third parties.

License Agreement with Novartis

In March 2017, we entered into a license agreement with Novartis, pursuant to which we were granted an exclusive, field-restricted, worldwide license to certain intellectual property rights owned or controlled by Novartis, including patents, patent applications, proprietary information, know-how and other intellectual property, to develop, commercialize and sell one or more therapeutic products comprising RTB101 alone or RTB101 and everolimus in a fixed dose combination. Under the license agreement, we have been licensed a patent portfolio of ten patent families directed to composition of matter of RTB101 and its salts, formulations of everolimus and methods of using RTB101 and everolimus to enhance the immune response among others. These families include certain granted patents and pending patent applications

in the United States and foreign jurisdictions, including Canada, the United Kingdom, Germany, France, Italy, Spain, Russia, Japan, Korea and China. Patents in these families will begin expiring in 2026, subject to possible patent term extensions. We believe that patent term extension and the potential grant of certain pending patent application may provide exclusivity for RTB101 and RTB101+everolimus combination until 2036 in the United States and the major European markets.

The exclusive field for RTB101 is for the treatment, prevention and diagnosis of diseases and other conditions in all indications in humans and animals. With respect to the fixed dose combination of RTB101 and everolimus, the exclusive field of use is for any indication in humans related to the improvement in immune function or immunosenescence in the elderly, the reduction of infection frequency, severity, duration, health care resource utilization, hospitalization, morbidity or mortality, or the treatment of infections, the reduction of pulmonary disease exacerbation frequency, severity, or related hospitalization, the enhancement of therapeutic or prophylactic benefits of vaccines, or any aging-related disease, excluding in each case the application of everolimus in connection with organ transplantation, oncology, immune-oncology or in the cardiac stent field. Novartis has agreed not to enforce any rights to improvements related to RTB101 developed after the effective date in connection with the exercise of our rights under this agreement. In addition, we have agreed to grant back to Novartis for use outside of the exclusive fields any improvements related to everolimus that we develop after the effective date.

We are required to use commercially reasonable efforts to develop and commercialize at least one product in the field in at least one major market, which includes the United States, Japan and certain identified countries in Europe.

As initial consideration for the license, we issued NIBR 2,587,992 shares of our Series A preferred stock.

As additional consideration for the license, we are required to pay up to an aggregate of $4.3 million upon the satisfaction of clinical milestones, up to an aggregate of $24 million upon the satisfaction of regulatory milestones for the first indication approved, and up to an aggregate of $18 million upon the satisfaction of regulatory milestones for the second indication approved. In addition, we are required to pay up to an aggregate of $125 million upon the satisfaction of commercial milestones, based on the amount of annual net sales. We are also required to pay tiered royalties ranging from a mid-single digit percentage to a low-teen digit percentage on annual net sales of products. These royalty obligations last on a product-by-product and country-by-country basis until the latest of (i) the expiration of the last valid claim of a Novartis patent covering a subject product, (ii) the expiration of any regulatory exclusivity for the subject product in a country, or (iii) the 10th anniversary of the first commercial sale of the product in the country, and are subject to a reduction after the expiration of the last valid claim of a Novartis patent or the introduction of a generic equivalent of a product in a country. In addition, if we sublicense the rights under the license agreement, we are required to pay a certain percentage of the sublicense revenue to Novartis. Novartis will no longer be entitled to sublicense revenue following the last visit of the 400th subject in any human clinical trial conducted by us or a sublicensee of ours, which we expect to occur by the end of our ongoing Phase 2b clinical trial.

Either we or Novartis may terminate the license agreement if the other party commits a material breach and fails to cure such breach within 60 days after written notice. Novartis may terminate the license agreement upon our bankruptcy, insolvency, dissolution or winding up. In addition, Novartis may partially terminate the license agreement with respect to everolimus if we fail or cease to use commercially reasonable efforts to research, develop and commercialize a product utilizing everolimus for a period of three years, provided that our license related to RTB101 and Novartis's license to our improvements related to everolimus will continue. In addition, we may terminate the license agreement, with or without cause, in its entirety or on a product-by-product or country-by-country basis, upon 60 days' prior written notice.

In connection with the license agreement, NIBR entered into certain stockholder agreements related to this investment. See "Certain Relationship and Related Party Transactions—Series A Preferred Stock Financing."

Sales and Marketing

We hold worldwide commercialization rights to our product candidates. We do not have our own marketing, sales or distribution capabilities. In order to commercialize our product candidate if approved for commercial sale, we must either develop a sales and marketing infrastructure or collaborate with third parties that have sales and marketing experience. We plan to directly commercialize our product candidates in the United States with a focused sales force targeting top-prescribing physicians with high flow of elderly patients. For some indications, we may also directly commercialize our product candidates in the European Union. In other markets or for certain indications outside the United States for which commercialization may be less capital efficient for us, we may selectively pursue strategic collaborations with third parties in order to maximize the commercial potential of our product candidates.

Manufacturing

RTB101 and everolimus are small molecules that can be manufactured using commercially available technologies. We acquired data from Novartis related to the chemical synthesis and manufacturing of RTB101, which is currently being manufactured by a single contract manufacturing organization, and are outsourcing the manufacturing of everolimus.

We believe there are multiple sources for all of the materials required for the manufacture of our product candidates. Our manufacturing strategy enables us to more efficiently direct financial resources to the research, development, and commercialization of product candidates rather than diverting resources to internally develop manufacturing facilities. As our product candidates advance through development, we expect to enter into longer-term commercial supply agreements with key suppliers and manufacturers to fulfill and secure the ongoing and planned preclinical, clinical, and, if our product candidates are approved for marketing, our commercial supply needs for ourselves and our collaborators. Our long-term strategy is to secure at least two sources for the manufacturing of our products.

Manufacturing of any product candidate is subject to extensive regulations that impose various procedural and documentation requirements, which govern recordkeeping, manufacturing processes and controls, personnel, quality control and quality assurance, among others. We expect that all of our contract manufacturing organizations will manufacture RTB101 under current Good Manufacturing Practice, or cGMP, conditions. cGMP is a regulatory standard for the production of pharmaceuticals to be used in humans.

Competition

We consider Navitor Pharma to be our most direct competitor in developing novel therapeutics targeting TORC1 for aging-related diseases. However, Navitor has not publicly announced testing of any pipeline candidate in human subjects to date. We are aware of multiple other allosteric and catalytic mTOR inhibitors in development by other companies. We are not aware of any product with comparable TORC1 selectivity being commercially developed.

We are also aware of other companies seeking to develop treatments to prevent or treat aging-related diseases through biological pathways unrelated to mTOR inhibition, including Calico and Unity. Calico has not yet disclosed any pipeline candidates, and Unity's most advanced candidate, based on publicly disclosed information, is in preclinical development. Hence, we believe that we currently have the most clinically advanced program based on the stage of development of our competitors' programs.

We are aware of other companies that are potential competitors for prevention or treatment of respiratory tract infections. Companies pursuing broad-spectrum prophylactic and therapeutic treatments in respiratory tract infections include PrEP BioPharm and Innavac. Based on publicly disclosed information, we believe that we have the most clinically advanced program, and the only program based on TORC1 selectivity. Narrow-spectrum prophylactic treatments are also being developed by potential competitors. Several of these treatments target the respiratory syncytial virus, or RSV, one of the top known causes of RTIs in older adults. However, as RTIs in the elderly are largely caused by many different viruses, we believe that our approach may be more broadly applicable in addressing RTIs.

Drug development is highly competitive and subject to rapid and significant technological advancements. Our ability to compete will significantly depend upon our ability to complete necessary clinical trials and regulatory approval processes, and effectively market any drug that we may successfully develop. Our current and potential future competitors may include pharmaceutical and biotechnology companies, academic institutions and government agencies. The primary competitive factors that will affect the commercial success of any product candidate for which we may receive regulatory approval include efficacy, safety and tolerability profile, dosing convenience, price, formulary coverage and reimbursement. Our existing or potential future competitors may have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of product candidates, as well as in obtaining regulatory approvals of those product candidates in the United States and in foreign countries. Our current and potential future competitors may also have significantly more experience commercializing drugs that have been approved for marketing. Mergers and acquisitions in the pharmaceutical and biotechnology industries could result in even more resources being concentrated among a small number of our competitors.

Accordingly, our competitors may be more successful than us in obtaining regulatory approval for therapies and in achieving widespread market acceptance of their drugs. It is also possible that the development of a more effective treatment method for prevention of respiratory tract infections by a competitor could render our product candidate non-competitive or obsolete or reduce the demand for our product candidate before we can recover our development and commercialization expenses.

Government Regulation

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of pharmaceutical products. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

Review and Approval of Drugs in the United States

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations. The failure to comply with applicable U.S. requirements at any time during the product development process, approval process or after approval may subject an applicant and/or sponsor to a variety of administrative or judicial sanctions, including refusal by the FDA to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of letters, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by the FDA and the Department of Justice or other governmental entities. In addition, an applicant may need to recall a product.

An applicant seeking approval to market and distribute a new drug product in the United States must typically undertake the following:

- completion of nonclinical, or preclinical, laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;
- submission to the FDA of an IND, which must take effect before human clinical trials may begin;
- approval by an independent Institutional Review Board, or IRB, representing each clinical site before each clinical trial may be initiated at that site;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed drug product for each indication;
- preparation and submission to the FDA of a new drug application, or NDA, and payment of user fees;
- review of the product by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with current Good Manufacturing Practices, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data;
- FDA review and approval of the NDA; and
- compliance with any post-approval requirements, including Risk Evaluation and Mitigation Strategies, or REMS, and post-approval studies required by the FDA.

Preclinical Studies

Before an applicant begins testing a compound in humans, the drug candidate enters the preclinical testing stage. Preclinical studies include laboratory evaluation of the purity and stability of the manufactured drug substance or active pharmaceutical ingredient and the formulated drug or drug product, as well as in vitro and animal studies to assess the safety

and activity of the drug for initial testing in humans and to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations. The results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted.

The IND and IRB Processes

An IND is an exemption from the FDCA that allows an unapproved drug to be shipped in interstate commerce for use in an investigational clinical trial and a request for FDA authorization to administer such investigational drug to humans. Such authorization must be secured prior to interstate shipment and administration of the investigational drug. In an IND, applicants must submit a protocol for each clinical trial and any subsequent protocol amendments. In addition, the results of the preclinical tests, manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, are submitted to the FDA as part of an IND. The FDA requires a 30-day waiting period after the filing of each IND before clinical trials may begin. At any time during this 30-day period, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin.

Following commencement of a clinical trial under an IND, the FDA may also place a clinical hold or partial clinical hold on that trial. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. No more than 30 days after imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold.

Following issuance of a clinical hold or partial clinical hold, an investigation may only resume after the FDA has notified the sponsor that the investigation may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed.

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all FDA IND requirements must be met unless waived. When the foreign clinical study is not conducted under an IND, the sponsor must ensure that the study is conducted in accordance with good clinical practice, or GCP, including review and approval by an independent ethics committee, or IEC, and informed consent from subjects. The GCP requirements are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies, as well as the quality and integrity of the resulting data. FDA must also be able to validate the data from the study through an on-site inspection if necessary.

In addition to the foregoing IND requirements, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review of the study at least annually. 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. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access that only the group maintains to available data from the study. Suspension or termination of development during any phase of clinical trials can occur if it is determined that the subjects or patients are being exposed to an unacceptable health risk. Other reasons for suspension or termination may be made by us based on evolving business objectives and/or competitive climate.

Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health, or NIH, for public dissemination on its ClinicalTrials.gov website.

Human Clinical Trials in Support of an NDA

Clinical trials involve the administration of the investigational 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 trial. Clinical trials are conducted under written study protocols detailing, among other things, the inclusion and exclusion criteria, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated.

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

- *Phase 1.* The drug is initially introduced into healthy human subjects or, in certain indications such as cancer, 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 and to determine optimal dosage.

- *Phase 2.* The drug 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 is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to evaluate 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.

- *Phase 4.* Post-approval studies may be conducted after initial regulatory approval. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or in vitro testing that suggest a significant risk in humans exposed to the drug; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

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

Review of an NDA by the FDA

Assuming successful completion of required clinical testing and other requirements, the results of the preclinical studies and clinical trials, 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 requesting approval to market the drug product for one or more indications. Under federal law, the submission of most NDAs is additionally subject to an application user fee, currently exceeding $2.4 million for applications requiring clinical data, and an annual prescription drug program fee exceeding $304,000. These fees are typically increased annually. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for drugs with orphan designation.

The FDA conducts a preliminary review of an NDA within 60 days of its receipt, before accepting the NDA for filing, to determine whether the application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA 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 process of NDAs. Applications for drugs containing novel active moieties are meant to be reviewed within ten months from the date of filing, and applications for "priority review" products containing novel active moieties are meant to be reviewed within six months of filing. The review process may be extended by the FDA for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections may cover all facilities associated with an NDA submission, including drug component manufacturing (such as active pharmaceutical ingredients), finished drug product manufacturing, and control testing laboratories. 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, as a condition of approval, the FDA may require an applicant to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential adverse events, and whether the product is a new molecular entity. REMS can include medication guides, physician communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU may include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The FDA may require a REMS before approval or post-approval if it becomes aware of a serious risk associated with use of the product. The requirement for a REMS can materially affect the potential market and profitability of a product.

The FDA is required to refer an application for a novel drug to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Fast Track, Breakthrough Therapy, and Priority Review

The FDA has a number of programs intended to facilitate and expedite development and review of new drugs if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. Three of these programs are referred to as fast track designation, breakthrough therapy designation, and priority review designation.

Specifically, the FDA may designate a product for Fast Track review if it is intended, whether alone or in combination with one or more other products, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For Fast Track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a Fast Track product's application before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a Fast Track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay 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 application 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 trial process.

Second, a product may be designated as a Breakthrough Therapy if it is intended, either alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the 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. The FDA may take certain actions with respect to Breakthrough Therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

Third, the FDA may designate a product for priority review if it is a product that treats a serious or life-threatening disease or condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed product represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a product for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Products granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a product, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints, but has indicated that such endpoints generally may support accelerated approval where the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a product.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a product, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly.

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the product's clinical benefit. As a result, 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 trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, could result in the FDA's withdrawal of the approval and require the withdrawal of the product from the market on an expedited basis. All promotional materials for product candidates approved under accelerated regulations are subject to prior review by the FDA.

The FDA's Decision on an NDA

On the basis of the FDA's evaluation of the NDA and accompanying information, including the results of the inspection of the manufacturing facilities and select clinical trial sites, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter 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, 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. 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 trials, be conducted to further assess the drug's safety or effectiveness after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are 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, many changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are annual program fee requirements for certain marketed products.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials, 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 the NDA holder and any third-party manufacturers that the NDA holder may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area 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 trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS 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 voluntary product recalls;
- fines, warning or untitled letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- 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 may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution.

Hatch-Waxman Amendments

Section 505 of the FDCA describes three types of marketing applications that may be submitted to the FDA to request marketing authorization for a new drug. A Section 505(b)(1) NDA is an application that contains full reports of investigations of safety and efficacy. A 505(b)(2) NDA is an application that contains full reports of investigations of safety and efficacy but where at least some of the information required for approval comes from investigations that were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted. This regulatory pathway enables the applicant to rely, in part, on the FDA's prior findings of safety and efficacy for an existing product, or published literature, in support of its application.

Section 505(j) establishes an abbreviated approval process for a generic version of approved drug products through the submission of an Abbreviated New Drug Application, or ANDA. An ANDA provides for marketing of a generic drug product that has the same active ingredients, dosage form, strength, route of administration, labeling, performance characteristics and intended use, among other things, to a previously approved product, known as a reference listed drug, or RLD. ANDAs are termed "abbreviated" because they are generally not required to include preclinical (animal) and clinical (human) data to establish safety and efficacy. Instead, generic applicants must scientifically demonstrate that their product is bioequivalent to, or performs in the same manner as, the innovator drug through in vitro, in vivo, or other testing. The generic version must deliver the same amount of active ingredients into a subject's bloodstream in the same amount of time as the innovator drug and can often be substituted by pharmacists under prescriptions written for the reference listed drug.

Non-Patent Exclusivity

Under the Hatch-Waxman Amendments, the FDA may not approve (or in some cases accept) an ANDA or 505(b)(2) application until any applicable period of non-patent exclusivity for the RLD has expired. The FDCA provides a period of five years of non-patent data exclusivity for a new drug containing a new chemical entity, or NCE. For the purposes of this provision, an NCE is a drug that contains no active moiety that has previously been approved by the FDA in any other NDA. An active moiety is the molecule or ion responsible for the physiological or pharmacological action of the drug substance. In cases where such NCE exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, which states the proposed generic drug will not infringe one or more of the already approved product's listed patents or that such patents are invalid or unenforceable, in which case the applicant may submit its application four years following the original product approval.

The FDCA also provides for a period of three years of exclusivity for non-NCE drugs if the NDA or a supplement to the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application or supplement. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication, but it generally would not protect the original, unmodified product from generic competition. Unlike five-year NCE exclusivity, an award of three-year exclusivity does not block the FDA from accepting ANDAs seeking approval for generic versions of the drug as of the date of approval of the original drug product; it only prevents FDA from approving such ANDAs.

Hatch-Waxman Patent Certification and the 30-Month Stay

In seeking approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or an approved method of using the product. Upon approval, each of the patents listed by the NDA sponsor is published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Upon submission of an ANDA or 505(b)(2) NDA, an applicant is required to certify to the FDA concerning any patents listed for the RLD in the Orange Book that:

- no patent information on the drug product that is the subject of the application has been submitted to the FDA;
- such patent has expired;
- the date on which such patent expires; or
- such patent is invalid, unenforceable or will not be infringed upon by the manufacture, use, or sale of the drug product for which the application is submitted.

Generally, the ANDA or 505(b)(2) NDA cannot be approved until all listed patents have expired, except where the ANDA or 505(b)(2) NDA applicant challenges a listed patent through the last type of certification, also known as a paragraph IV certification. If the applicant does not challenge the listed patents or indicates that it is not seeking approval of a patented method of use, the ANDA or 505(b)(2) NDA application will not be approved until all of the listed patents claiming the referenced product have expired. If the ANDA or 505(b)(2) NDA applicant has provided a paragraph IV certification the applicant must send notice of the paragraph IV certification to the NDA and patent holders once the application has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the paragraph IV certification. If the paragraph IV certification is challenged by an NDA holder or the patent owner(s) asserts a patent challenge to the paragraph IV certification, the FDA may not approve that application until the earlier of 30 months from the receipt of the notice of the paragraph IV certification, the expiration of the patent, when the

infringement case concerning each such patent was favorably decided in the applicant's favor or settled, or such shorter or longer period as may be ordered by a court. This prohibition is generally referred to as the 30-month stay. In instances where an ANDA or 505(b)(2) NDA applicant files a paragraph IV certification, the NDA holder or patent owner(s) regularly take action to trigger the 30-month stay, recognizing that the related patent litigation may take many months or years to resolve. Thus, approval of an ANDA or 505(b)(2) NDA could be delayed for a significant period of time depending on the patent certification the applicant makes and the reference drug sponsor's decision to initiate patent litigation. If the drug has NCE exclusivity and the ANDA is submitted four years after approval, the 30-month stay is extended so that it expires 7 ½ years after approval of the innovator drug, unless the patent expires or there is a decision in the infringement case that is favorable to the ANDA applicant before then.

Pediatric Studies and Exclusivity

Under the Pediatric Research Equity Act of 2003, a NDA or supplement thereto for a drug with certain innovative features (*e.g.*, new active ingredient, new indication, new dosage form) must contain data that are adequate to assess the safety and effectiveness of the drug 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. With enactment of the Food and Drug Administration Safety and Innovation Act, or FDASIA, in 2012, sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The applicant, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

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. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation.

Pediatric exclusivity is another type of non-patent exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of certain existing non-patent exclusivity periods, including orphan exclusivity. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data within certain time periods. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application after expiration of a patent.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition (generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a drug product available in the United States for treatment of the disease or condition will be recovered from sales of the product). A company must request orphan product designation before submitting an NDA. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product with orphan status receives the first FDA approval for the drug for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will receive orphan product exclusivity. Orphan product exclusivity means that the FDA may not approve any other applications for the same product for the same indication for seven years, except in certain limited circumstances. Competitors may receive approval of different products for the indication for which the orphan product has exclusivity and may obtain approval for the same product but for a different indication. If a drug or drug product designated as an orphan product ultimately receives regulatory approval for an indication broader than what was designated in its orphan product application, it may not be entitled to exclusivity.

Patent Term Restoration and Extension

A patent claiming a new drug product may be eligible for a limited patent term extension under the Hatch-Waxman Amendments, which permits a patent term restoration of up to five years for patent term lost during product development and the FDA regulatory review. The restoration period granted is typically one-half the time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of an NDA and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved drug product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question and within 60 days of drug approval. A patent that covers multiple drugs for which approval is sought can only be extended in connection with one of the approvals. The U.S. Patent and Trademark Office reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Review and Approval of Medicinal Products in the European Union

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of products. Whether or not it obtains FDA approval for a product, an applicant will need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. Specifically, the process governing approval of medicinal products in the European Union generally follows the same lines as in the United States. It entails satisfactory completion of preclinical studies and adequate and well-controlled clinical trials to establish the safety and efficacy of the product for each proposed indication. It also requires the submission to the relevant competent authorities of a marketing authorization application, or MAA, and granting of a marketing authorization by these authorities before the product can be marketed and sold in the European Union.

Clinical Trial Approval

The Clinical Trials Directive 2001/20/EC, the Directive 2005/28/EC on Good Clinical Practice, or GCP, and the related national implementing provisions of the individual EU Member States govern the system for the approval of clinical trials in the European Union. Under this system, an applicant must obtain prior approval from the competent national authority of the EU Member States in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial at a specific study site after the competent ethics committee has issued a favorable opinion. The clinical trial application must be accompanied by, among other documents, an investigational medicinal product dossier (the Common Technical Document) with supporting information prescribed by Directive 2001/20/EC, Directive 2005/28/EC, where relevant the implementing national provisions of the individual EU Member States and further detailed in applicable guidance documents.

In April 2014, the new Clinical Trials Regulation, (EU) No 536/2014 (Clinical Trials Regulation) was adopted. The Regulation is anticipated to apply in 2019. The Clinical Trials Regulation will be directly applicable in all the EU Member States, repealing the current Clinical Trials Directive 2001/20/EC. Conduct of all clinical trials performed in the European Union will continue to be bound by currently applicable provisions until the new Clinical Trials Regulation becomes applicable. The extent to which ongoing clinical trials will be governed by the Clinical Trials Regulation will depend on when the Clinical Trials Regulation becomes applicable and on the duration of the individual clinical trial. If a clinical trial continues for more than three years from the day on which the Clinical Trials Regulation becomes applicable the Clinical Trials Regulation will at that time begin to apply to the clinical trial.

The new Clinical Trials Regulation aims to simplify and streamline the approval of clinical trials in the European Union. The main characteristics of the regulation include: a streamlined application procedure via a single entry point, the "EU portal"; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is assessed by the competent authorities of all EU Member States in which an application for authorization of a clinical trial has been submitted (Member States concerned). Part II is assessed separately by each Member State concerned. Strict deadlines have been established for the assessment of clinical trial applications. The role of the relevant ethics committees in the assessment procedure will continue to be governed by the national law of the concerned EU Member State. However, overall related timelines will be defined by the Clinical Trials Regulation.

Marketing Authorization

To obtain a marketing authorization for a product under European Union regulatory systems, an applicant must submit an MAA either under a centralized procedure administered by the European Medicines Agency, or EMA, or one of the procedures administered by competent authorities in the EU Member States (decentralized procedure or mutual recognition procedure). A marketing authorization may be granted only to an applicant established in the European Union. Regulation (EC) No 1901/2006 provides that prior to obtaining a marketing authorization in the European Union, applicants have to demonstrate compliance with all measures included in an EMA-approved Pediatric Investigation Plan, or PIP, covering all subsets of the pediatric population, unless the EMA has granted (1) a product-specific waiver, (2) a class waiver or (3) a deferral for one or more of the measures included in the PIP.

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid for all EU Member States and three of the four European Free Trade Association, or EFTA, States, Iceland, Liechtenstein and Norway. Pursuant to Regulation (EC) No 726/2004, the centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy products and products with a new active substance indicated for the treatment of certain diseases, including products for the treatment of HIV or AIDS, cancer, diabetes, neurodegenerative diseases, auto-immune and other immune dysfunctions and viral diseases. For products with a new active substance indicated for the treatment of other diseases and products that are a significant therapeutic, scientific or technical innovation and whose authorization would be in the interest of public health at EU level, the centralized procedure is optional.

Under the centralized procedure, the Committee for Medicinal Products for Human Use, or the CHMP, established at the EMA is responsible for conducting the initial assessment of a product. The CHMP is also responsible for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the applicant in response to questions of the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. If the CHMP accepts such request, the time limit of 210 days will be reduced to 150 days, but it is possible that the CHMP can revert to the standard time limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment. At the end of this period, the CHMP provides a scientific opinion on whether or not a marketing authorization should be granted in relation to a medicinal product. Within 67 days from the date of the CHMP Opinion, the European Commission will adopt its final decision on the marketing authorization application.

Unlike the centralized authorization procedure, the decentralized marketing authorization procedure requires a separate application to, and leads to separate approval by, the competent authorities of each EU Member State in which the product is to be marketed. This application is identical to the application that would be submitted to the EMA for authorization through the centralized procedure. The reference EU Member State prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. The resulting assessment report is submitted to the concerned EU Member States who, within 90 days of receipt, must decide whether to approve the assessment report and related materials. If a concerned EU Member State cannot approve the assessment report and related materials due to concerns relating to a potential serious risk to public health, disputed elements may be referred to the European Commission, whose decision is binding on all EU Member States.

The mutual recognition procedure similarly is based on the acceptance by the competent authorities of the EU Member States of the marketing authorization of a medicinal product by the competent authorities of other EU Member States. The holder of a national marketing authorization may submit an application to the competent authority of an EU Member State requesting that this authority recognize the marketing authorization delivered by the competent authority of another EU Member State.

Regulatory Data Protection in the European Union

In the European Union, innovative medicinal products approved on the basis of a complete independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity pursuant to Directive 2001/83/EC. Regulation (EC) No 726/2004 repeats this entitlement for medicinal products authorized in accordance the centralized authorization procedure. Data exclusivity prevents applicants for authorization of generics of these innovative products from referencing the innovator’s data to assess a generic (abbreviated) application for a period of eight years. During an additional two-year period of market exclusivity, a generic marketing authorization application can be submitted and authorized, and the innovator’s data may be referenced, but no generic medicinal product can be placed on the European Union market until the expiration of the market exclusivity. The overall ten-year period will

be extended to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. Even if a compound is considered to be a new chemical entity so that the innovator gains the prescribed period of data exclusivity, another company nevertheless could also market another version of the product if such company obtained marketing authorization based on an MAA with a complete independent data package of pharmaceutical tests, preclinical tests and clinical trials.

Periods of Authorization and Renewals

A marketing authorization has an initial validity for five years in principle. The marketing authorization may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA or by the competent authority of the EU Member State. To this end, the marketing authorization holder must provide the EMA or the competent authority with a consolidated version of the file in respect of quality, safety and efficacy, including all variations introduced since the marketing authorization was granted, at least six months before the marketing authorization ceases to be valid. The European Commission or the competent authorities of the EU Member States may decide, on justified grounds relating to pharmacovigilance, to proceed with one further five year period of marketing authorization. Once subsequently definitively renewed, the marketing authorization shall be valid for an unlimited period. Any authorization which is not followed by the actual placing of the medicinal product on the European Union market (in case of centralized procedure) or on the market of the authorizing EU Member State within three years after authorization ceases to be valid (the so-called sunset clause).

Regulatory Requirements after a Marketing Authorization has been Obtained

In case an authorization for a medicinal product in the European Union is obtained, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include:

- Compliance with the European Union's stringent pharmacovigilance or safety reporting rules must be ensured. These rules can impose post-authorization studies and additional monitoring obligations.

- The manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the applicable European Union laws, regulations and guidance, including Directive 2001/83/EC, Directive 2003/94/EC, Regulation (EC) No 726/2004 and the European Commission Guidelines for Good Manufacturing Practice. These requirements include compliance with European Union cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the European Union with the intention to import the active pharmaceutical ingredients into the European Union.

- The marketing and promotion of authorized drugs, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the European Union notably under Directive 2001/83/EC, as amended, and EU Member State laws.

Brexit and the Regulatory Framework in the United Kingdom

On June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union (commonly referred to as "Brexit"). Thereafter, on March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. The withdrawal of the United Kingdom from the European Union will take effect either on the effective date of the withdrawal agreement or, in the absence of agreement, two years after the United Kingdom provides a notice of withdrawal pursuant to the EU Treaty. Since the regulatory framework for pharmaceutical products in the United Kingdom covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from European Union directives and regulations, Brexit could materially impact the future regulatory regime which applies to products and the approval of product candidates in the United Kingdom. It remains to be seen how, if at all, Brexit will impact regulatory requirements for product candidates and products in the United Kingdom.

Healthcare Law and Regulation

Healthcare providers and third-party payors play a primary role in the recommendation and prescription of drug products that are granted regulatory approval. Arrangements with providers, consultants, third-party payors and customers

are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, reporting of payments to physicians and teaching hospitals and patient privacy laws and regulations and other healthcare laws and regulations that may constrain our business and/or financial arrangements. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid; a person or entity need not have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it in order to have committed a violation; in addition, the government may assert that a claim that includes 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;

- the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious or fraudulent; knowingly 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;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal laws that prohibit, among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or 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; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, which impose obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- the federal transparency requirements known as the federal Physician Payments Sunshine Act, under the Patient Protection and Affordable Care Act, as amended by the Health Care Education Reconciliation Act, or the Affordable Care Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within the United States Department of Health and Human Services, information related to payments and other transfers of value made by that entity to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to healthcare items or services that are reimbursed by non-governmental third-party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry’s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures and pricing information. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Pharmaceutical Insurance Coverage and Healthcare Reform

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Thus, even if a product candidate is approved, sales of the product will depend, in part, on the extent to

which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage, and establish adequate reimbursement levels for, the product. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable regulatory approvals. Additionally, companies may also need to provide discounts to purchasers, private health plans or government healthcare programs. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product could reduce physician utilization once the product is approved and have a material adverse effect on sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage 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 products have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical products, limiting coverage and the amount of reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the United States. For example, in March 2010, the United States Congress enacted the Affordable Care Act, which, among other things, includes changes to the coverage and payment for products under government health care programs. Among the provisions of the Affordable Care Act of importance to our potential product candidates are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic products, apportioned among these entities according to their market share in certain government healthcare programs;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price," or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices;
- addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- expanded the types of entities eligible for the 340B drug discount program;
- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 50% point-of-sale-discount off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D; 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.

Other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2025 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, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. In addition, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their commercial products, which has resulted in several Congressional inquiries and proposed bills designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for pharmaceutical products. Individual states in the United States have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

On January 20, 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the Affordable Care Act to waive, defer, grant exemptions from, or delay the implementation of any provision of the Affordable Care Act that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. Further legislative changes to or regulatory changes under the Affordable Care Act remain possible in the 115th U.S. Congress and under the Trump Administration. The nature and extent of any legislative or regulatory changes to the Affordable Care Act are uncertain at this time, however.

Outside the United States, ensuring coverage and adequate payment for a product also involves challenges. Pricing of prescription pharmaceuticals is subject to government control in many countries. Pricing negotiations with government authorities can extend well beyond the receipt of regulatory approval for a product and may require a clinical trial that compares the cost-effectiveness of a product to other available therapies. The conduct of such a clinical trial could be expensive and result in delays in commercialization.

In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that 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 or so-called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the European Union provides options for its member states to restrict the range of 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 product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other member states allow companies to fix their own prices for products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the European Union have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage healthcare expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the European Union. The downward pressure on healthcare costs in general, particularly prescription products, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states, and parallel trade, i.e., arbitrage between low-priced and high-priced member states, can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any products, if approved in those countries.

Employees

As of March 23, 2018, we had seven full-time employees, including a total of three employees with M.D. or Ph.D. degrees. Of our workforce, four employees are directly engaged in research and development activities, and three employees provide administrative, business and operations support. None of our employees are represented by labor unions or covered

by collective bargaining agreements. We consider the relationship with our employees to be good. We also use outside consultants and contractors for limited engagements.

Legal Proceedings

We are not currently subject to any material legal proceedings.

Corporate Information

We were incorporated under the laws of the State of Delaware in July 2016. Our principal offices are located at 500 Boylston Street, 12th floor, Boston, MA 02116, and our telephone number is (617) 482-2333. Our website address is www.restorbio.com. Our website and the information contained on, or that can be accessed through, the website will not be deemed to be incorporated by reference in, and are not considered part of, this Annual Report on Form 10-K. You should not rely on any such information in making your decision whether to purchase our common stock.

Available Information

We file annual, quarterly, and current reports, proxy statements, and other documents with the Securities and Exchange Commission (SEC) under the Securities Exchange Act of 1934, as amended (the Exchange Act). The public may read and copy any materials that we file with the SEC at the SEC's Public Reference Room at 100 F Street, NE, Washington, DC 20549. The public may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. Also, the SEC maintains an Internet website that contains reports, proxy and information statements, and other information regarding issuers, including us, that file electronically with the SEC. The public can obtain any documents that we file with the SEC at www.sec.gov.

Copies of each of our filings with the SEC on Form 10-K, Form 10-Q and Form 8-K and all amendments to those reports, can be viewed and downloaded free of charge at our website, www.restorbio.com after the reports and amendments are electronically filed with, or otherwise furnished to, the SEC.

Our code of conduct, corporate governance guidelines and the charters of our Audit Committee, Compensation Committee and Nominating and Corporate Governance Committee are available through our website at www.restorbio.com.

Item 1A. Risk Factors.

Investing in our common stock involves a high degree of risk. You should carefully consider the following risks and uncertainties, together with all other information in this Annual Report on Form 10-K, including our consolidated financial statements and related notes and "Management's Discussion and Analysis of Results of Operations and Financial Condition," as well as our other filings with the Securities and Exchange Commission, before investing in our common stock. Any of the risk factors we describe below could adversely affect our business, financial condition or results of operations. The market price of our common stock could decline if one or more of these risks or uncertainties actually occur, causing you to lose all or part of your investment in our common stock. The risks and uncertainties we describe below are not the only ones we face. Additional risks and uncertainties that we currently do not know about or that we currently believe to be immaterial may also impair our business. Certain statements below are forward-looking statements. See "Special Note Regarding Forward-Looking Statements and Industry Data" in this Annual Report on Form 10-K.

Risks Related to Our Financial Position and Need for Capital

We have incurred significant losses since our inception. We anticipate that we will continue to incur significant losses for the foreseeable future, and we may never achieve or maintain profitability.

We are a clinical-stage biopharmaceutical company with a limited operating history. Investment in biopharmaceutical product development is highly speculative because it entails substantial upfront capital expenditures and significant risk that any potential product candidate will fail to demonstrate adequate effect or an acceptable safety profile, gain regulatory approval and become commercially viable. We have no products approved for commercial sale and have not generated any revenue from product sales to date, and we will continue to incur significant research and development and other expenses related to our ongoing operations. As a result, we are not profitable and have incurred losses in each period since our inception in July 2016. We have devoted a majority of our financial resources and efforts to research and development, including preclinical studies and our clinical trials. Our financial condition and operating results, including net losses, may fluctuate significantly from quarter to quarter and year to year. Accordingly, you should not rely upon the results of any quarterly or annual periods as indications of future operating performance. Additionally, net losses and negative cash flows have had, and will continue to have, an adverse effect on our stockholders' equity and working capital. For the period from July 5, 2016 (inception) to December 31, 2016, we reported a net loss of $1,000. For the year ended December 31, 2017, we reported a net loss of $33.8 million. As of December 31, 2017, we had an accumulated deficit of $33.8 million. We expect to continue to incur significant losses for the foreseeable future, and we expect these losses to increase as we continue our research and development of, and seek regulatory approvals for, RTB101, alone or in combination with everolimus, and other product candidates.

We anticipate that our expenses will increase substantially if and as we:

- continue to develop and conduct clinical trials for our lead product candidate, RTB101, alone and in combination with everolimus;
- initiate and continue research, preclinical and clinical development efforts for any current or future product candidates;
- seek to identify additional product candidates;
- seek regulatory approvals for RTB101, alone or in combination with everolimus, or any other product candidates that successfully complete clinical development, if any;
- establish sales, marketing, distribution, manufacturing, supply chain and other commercial infrastructure in the future to commercialize various products for which we may obtain regulatory approval, if any;
- require the manufacture of larger quantities of RTB101 alone or in fixed dose combination with everolimus for clinical development and, potentially, commercialization;
- maintain, expand and protect our intellectual property portfolio;
- hire and retain additional personnel, such as clinical, quality control, scientific and commercial personnel;

- add operational, financial and management information systems and personnel, including personnel to support our product development and help us comply with our obligations as a public company;

- add equipment and physical infrastructure to support our research and development; and

- acquire or in-license other product candidates and technologies.

Our ability to become and remain profitable depends on our ability to generate revenue. We do not expect to generate significant revenue unless and until we are, or any future collaborator is, able to obtain regulatory approval for, and successfully commercialize, RTB101, alone or in combination with everolimus, or any other product candidates. Successful commercialization will require achievement of key milestones, including demonstrating safety and efficacy in clinical trials, obtaining regulatory, including marketing, approval for these product candidates, manufacturing, marketing and selling those products for which we, or any of our future collaborators, may obtain regulatory approval, satisfying any post-marketing requirements and obtaining reimbursement for our products from private insurance or government payors. Because of the uncertainties and risks associated with these activities, we are unable to accurately and precisely predict the timing and amount of revenues, the extent of any further losses or if or when we might achieve profitability. We and any future collaborators may never succeed in these activities and, even if we do, or any future collaborators do, we may never generate revenues that are large enough for us to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Additionally, our expenses could increase if we are required by the U.S. Food and Drug Administration, or FDA, or any comparable foreign regulatory authority to perform studies in addition to those currently expected, or if there are any delays in completing our clinical trials or the development of any of our product candidates.

Our failure to become and remain profitable would depress the market price of our common stock and could impair our ability to raise capital, expand our business, diversify our product offerings or continue our operations. If we continue to suffer losses as we have in the past, investors may not receive any return on their investment and may lose their entire investment.

Our company has a limited operating history and no history of commercializing pharmaceutical products, which may make it difficult to evaluate the prospects for our future viability.

We were formed in July 2016 and commenced research and development operations in March 2017. Our operations to date have been limited to organizing, staffing and financing our company, raising capital, in-licensing our technology and conducting research and development activities for our product candidates. We have not yet demonstrated an ability to obtain regulatory approvals, manufacture a commercial-scale product, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Accordingly, you should consider our prospects in light of the costs, uncertainties, delays and difficulties frequently encountered by companies in clinical development, especially clinical-stage biopharmaceutical companies such as ours. Any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing pharmaceutical products.

We may encounter unforeseen expenses, difficulties, complications, delays and other known or unknown factors in achieving our business objectives. We will eventually need to transition from a company with a development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We will need substantial additional funding, and if we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product discovery and development programs or commercialization efforts.

Our operations have required substantial amounts of cash since inception. Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is a very time-consuming, expensive and uncertain process that takes years to complete. For the foreseeable future, we expect to continue to rely on additional financing to achieve our business objectives.

From July 5, 2016 (inception) to December 31, 2016, we did not use any cash for our operating activities, and for the year ended December 31, 2017, we used $11.0 million in net cash for our operating activities, of which a majority related to research and development activities. We expect our expenses to increase substantially in connection with our ongoing activities, particularly as we initiate new clinical trials of, initiate new research and preclinical development efforts for and seek regulatory approval for, RTB101, alone or in combination with everolimus, or any product candidates that we develop

or acquire, if any. In addition, if we obtain regulatory approval for RTB101, alone or in combination with everolimus, or any other product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Some of these expenses may be incurred in advance of regulatory approval, and could be substantial. Furthermore, following the completion of our initial public offering, or IPO, we expect to incur significant 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 may be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts.

We intend to use the net proceeds from our IPO, together with our existing cash and cash equivalents, to fund the development of RTB101, alone and in combination with everolimus, for RTIs and other indications, and of our TORC1 follow-on candidate and other pipeline candidates, and the remainder, if any, for working capital and general corporate purposes. We will be required to expend significant funds in order to advance the development of RTB101 alone and in combination with everolimus, as well as other product candidates we may seek to develop or acquire. In addition, while we may seek one or more collaborators for future development of RTB101 alone and in combination with everolimus for one or more additional indications beyond immunosenescence or in geographies outside of the United States, Europe and key territories, we may not be able to enter into a collaboration for RTB101 or any other product candidates for such indications or in such geographies on suitable terms, on a timely basis or at all. In any event, the net proceeds from our IPO and our existing cash and cash equivalents will not be sufficient to fund all of the efforts that we plan to undertake or to fund the completion of development of RTB101 alone or in combination with everolimus, including activities related to the development of RTB101, alone and in combination with everolimus, for RTIs and other indications, and the development of our TORC1 follow-on candidate and other pipeline candidates. Accordingly, we will be required to obtain substantial additional funding through public or private equity offerings, debt financings, collaborations and licensing arrangements or other sources.

We cannot be certain that additional funding will be available on acceptable terms, or at all. We have no committed source of additional capital and if we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of our product candidates or other research and development initiatives. Any of our current or future license agreements may also be terminated if we are unable to meet the payment or other obligations under the agreements. We could be required to seek collaborators for product candidates at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available or relinquish or license on unfavorable terms our rights to product candidates in markets where we otherwise would seek to pursue development or commercialization ourselves.

We believe that the net proceeds from our IPO, together with our existing cash and cash equivalents, will enable us to fund our operating expenses and capital expenditure requirements through 2020, including the completion of our ongoing Phase 2b clinical trial of RTB101 alone or in combination with everolimus, the completion of a subsequent pivotal Phase 3 clinical program, assuming a successful outcome in our Phase 2b clinical trial of RTB101 alone or in combination with everolimus, and the filing of a New Drug Application, or NDA, with the Food and Drug Administration, or FDA, assuming a successful outcome in our Phase 3 clinical program. Our estimate may prove to be wrong, and we could use our available capital resources sooner than we currently expect. Further, changing circumstances, some of which may be beyond our control, could cause us to consume capital significantly faster than we currently anticipate, and we may need to seek additional funds sooner than planned. Our future funding requirements, both short- and long-term, will depend on many factors, including:

- the scope, progress, timing, costs and results of clinical trials of, and research and preclinical development efforts for, RTB101, alone or in combination with everolimus, and any future product candidates;
- our ability to enter into, and the terms and timing of, any collaborations, licensing or other arrangements on favorable terms, if at all;
- the number of future product candidates that we pursue and their development requirements;
- the outcome, timing and costs of seeking regulatory approvals;
- if approved, the costs of commercialization activities for RTB101, alone or in combination with everolimus, or any other product candidate that receives regulatory approval to the extent such costs are not the responsibility of any future collaborators, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;

- subject to receipt of regulatory approval, revenue, if any, received from commercial sales of RTB101, alone or in combination with everolimus, or any future product candidates;

- the extent to which we in-license or acquire rights to other products, product candidates or technologies;

- our headcount growth and associated costs as we expand our research and development and establish a commercial infrastructure;

- the amount and timing of any payments we may be required to make, or that we may receive, in connection with the licensing, filing, prosecution, defense and enforcement of any patents or other intellectual property rights, including milestone and royalty payments and patent prosecution fees that we are obligated to pay pursuant to our license agreement;

- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights including enforcing and defending intellectual property related claims; and

- the costs of operating as a public company.

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

We expect our expenses to increase in connection with our planned operations. Unless and until we can generate a substantial amount of revenue from our product candidates, we expect to finance our future cash needs through public or private equity offerings, debt financings, collaborations, licensing arrangements or other sources, or any combination of the foregoing. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe that we have sufficient funds for our current or future operating plans.

To the extent that we raise additional capital through the sale of common stock, convertible securities or other equity securities, your ownership interest may be diluted, and the terms of these securities could include liquidation or other preferences and anti-dilution protections that could adversely affect your rights as a common stockholder. In addition, debt financing, if available, may result in fixed payment obligations and may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures, creating liens, redeeming stock or declaring dividends, that could adversely impact our ability to conduct our business. In addition, securing financing could require a substantial amount of time and attention from our management and may divert a disproportionate amount of their attention away from day-to-day activities, which may adversely affect our management's ability to oversee the development of our product candidates.

If we raise additional funds through collaborations or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds 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.

Our ability to use net operating losses and research and development credits to offset future taxable income may be subject to certain limitations.

As of December 31, 2017, we had federal and state net operating loss carryforwards of $14.5 million and $14.4 million, respectively, which begin to expire in various amounts in 2036. As of December 31, 2017, we also had federal research and development tax credit carryforwards of $0.2 million, which begin to expire in 2037. In general, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its pre-change net operating losses or tax credits, or NOLs or credits, to offset future taxable income or taxes. For these purposes, an ownership change generally occurs where the aggregate stock 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 specified testing period. Our existing NOLs or credits may be subject to limitations arising from previous ownership changes, and if we undergo an ownership change in connection with or after our IPO, our ability to utilize NOLs or credits could be further limited by Sections 382 and 383 of the Code. In addition, future changes in our stock ownership, many of which are outside of our control, could result in an ownership change under Sections 382 and 383 of the Code. Our NOLs or credits may also be

impaired under state law. Accordingly, we may not be able to utilize a material portion of our NOLs or credits. We have not completed a study to determine whether our IPO, our most recent private placement of our Series B preferred stock and other transactions that have occurred over the past three years may have triggered an ownership change limitation. If we determine that an ownership change has occurred and our ability to use our historical NOLs or credits is materially limited, it would harm our future operating results by effectively increasing our future tax obligations.

Furthermore, our ability to utilize our NOLs or credits is conditioned upon our attaining profitability and generating U. S. federal and state taxable income. As described above under "Risk Factors—Risks Related to our Financial Position and Need for Additional Capital," we have incurred significant net losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future; and therefore, we do not know whether or when we will generate the U.S. federal or state taxable income necessary to utilize our NOL or credit carryforwards that are subject to limitation by Sections 382 and 383 of the Code.

Comprehensive tax reform legislation could adversely affect our business and financial condition.

On December 22, 2017, President Trump signed into law the "Tax Cuts and Jobs Act", or TCJA, that significantly reforms the Internal Revenue Code of 1986, as amended, or the Code. The TCJA, among other things, includes changes to U.S. federal tax rates, imposes significant additional limitations on the deductibility or interest and net operating loss carryforwards, allows for the expensing of capital expenditures, and puts into effect the migration from a "worldwide" system of taxation to a territorial system. Our net deferred tax assets and liabilities will be revalued at the newly enacted U.S. corporate rate. We do not expect to recognize any tax expense in the year of enactment as our net deferred tax assets have a full valuation allowance recorded. We continue to examine the impact this tax reform legislation may have on our business. This Annual Report on Form 10-K does not discuss any such tax legislation or the manner in which it might affect purchasers of our common stock. We urge our stockholders to consult with their legal and tax advisors with respect to any such legislation and the potential tax consequences of investing in our common stock.

Risks Related to the Discovery, Development and Commercialization of Our Product Candidates

Our business depends virtually entirely upon the success of RTB101 alone or in combination with everolimus. If we are unable to obtain regulatory approval for or successfully commercialize RTB101, alone or in combination with everolimus, our business may be materially harmed.

We currently have no products approved for sale and are investing the majority of our efforts and financial resources in the development of our lead product candidate, RTB101, either alone or in combination with everolimus. Successful continued development and ultimate regulatory approval of RTB101, alone or in combination with everolimus, for the treatment of aging-related diseases, including our lead indication, reducing the incidence of respiratory tract infections, or RTIs, is critical to the future success of our business. We will need to raise sufficient funds for, and successfully enroll and complete, our clinical development program for RTB101, alone or in combination with everolimus, to treat RTIs and possibly other aging-related diseases. The future regulatory and commercial success of this product candidate is subject to a number of risks, including the following:

- we may not have sufficient financial and other resources to initiate or complete the necessary clinical trials for RTB101, alone or in combination with everolimus;
- we may not be able to obtain adequate evidence of clinical efficacy and safety for RTB101, alone or in combination with everolimus, or to obtain regulatory approval of RTB101, alone or in combination with everolimus, for reducing the incidence of RTIs or other indications;
- even if RTB101 monotherapy succeeds in its clinical development and is approved for one or more targeted indications, there can be no assurance that the RTB101+everolimus combination therapy would be developed successfully and approved, and vice versa;
- we may not be able to maintain an acceptable safety profile for RTB101 alone or in combination with everolimus, even if approved;
- we do not know the degree to which RTB101 alone or in combination with everolimus will have market uptake as a therapy by patients, the medical community or third-party payors, among others, if approved;

- in our clinical programs, we may experience variability in the response of subjects to treatment, the need to adjust clinical trial procedures and the need for additional clinical trial sites, which could delay our clinical trial progress;
- the results of our clinical trials may not meet the level of statistical significance required by the FDA, the European Medicines Agency, or EMA, or comparable foreign regulatory bodies for regulatory approval for reducing the incidence of RTIs or for other indications;
- we may have difficulty enrolling subjects in trials if, for instance, a current or future effective standard of care limits the desire of patients, physicians, or regulatory agencies to participate in or support clinical trials, or if patients choose to participate in the trials of other sponsors' product candidates;
- patients in our clinical trials may die or suffer other adverse effects for reasons that may or may not be related to RTB101, which could delay or prevent further clinical development;
- the requirements implemented by regulatory agencies may change at any time;
- the FDA, EMA or foreign regulatory agencies may require efficacy endpoints for a future clinical trial for reducing the incidence of RTIs that differ from the endpoints of our current or future trials, which may require us to conduct additional clinical trials;
- the mechanism of action of RTB101, alone or in combination with everolimus, is complex and we cannot guarantee the degree to which it will translate into a medical benefit in any indications;
- competitor products including generic products may be developed to reduce the incidence of RTIs that may have similar or better safety and efficacy or lower costs than RTB101 alone or in combination with everolimus;
- we may not be able to establish sales, marketing, distribution and other commercial infrastructure in the future to commercialize various products for which we may obtain regulatory approval;
- we or our contract manufacturers may not be able to manufacture RTB101, everolimus, the fixed dose combination of RTB101 with everolimus or other future product candidates at the appropriate quality or sufficient quantities to support further clinical development and/or commercialization;
- our investigational drug products or manufacturing processes may be considered by regulatory authorities, such as the FDA or EMA, to be unsuitable for continued development and/or commercialization;
- we may observe unexpected toxicities in preclinical safety or efficacy animal studies that delay, limit or prevent further clinical development;
- our intellectual property may not be patentable, valid or enforceable; and
- we may not be able to obtain, maintain, defend, protect or enforce our patents, our trade secrets, regulatory exclusivities and other intellectual property rights, both in the United States and internationally, including those that we have licensed under our license agreement with Novartis.

Many of these risks are beyond our control, including the risks related to clinical development, the regulatory submission process, potential threats to our intellectual property rights and the manufacturing, marketing and sales efforts of any future collaborator. If we are unable to develop, receive regulatory approval for, or successfully commercialize RTB101 alone or in combination with everolimus, or if we experience delays as a result of any of these risks or otherwise, our business could be materially harmed.

In addition, of the large number of drugs in development in the pharmaceutical industry, only a small percentage result in the submission of an NDA to the FDA and even fewer are approved for commercialization. Furthermore, even if we do receive regulatory approval for RTB101, alone or in combination with everolimus, any such approval may be subject to limitations on the indicated uses or patient populations for which we may market the product. Accordingly, even if we are

able to obtain the requisite financing to continue to fund our development programs, we cannot assure you that we will successfully develop or commercialize RTB101, alone or in combination with everolimus, for RTIs or any other indications. If we or any of our future collaborators are unable to develop, or obtain regulatory approval for, or, if approved, successfully commercialize RTB101, alone or in combination with everolimus, for RTIs or any other indications, we may not be able to generate sufficient revenue to continue our business.

We have no experience as a company in obtaining regulatory approval for a drug.

As a company, we have never obtained regulatory approval for, or commercialized, a drug. It is possible that the FDA may refuse to accept any or all of our planned NDAs for substantive review or may conclude after review of our data that our application is insufficient to obtain regulatory approval for any current or future product candidates. If the FDA does not approve any of our planned NDAs, it may require that we conduct additional costly clinical, nonclinical or manufacturing validation studies before it will reconsider our applications. Depending on the extent of these or any other FDA-required studies, approval of any NDA or other application that we submit may be significantly delayed, possibly for several years, or may require us to expend more resources than we have available. Any failure or delay in obtaining regulatory approvals would prevent us from commercializing RTB101 alone or in combination with everolimus or any other product candidate, generating revenues and achieving and sustaining profitability. It is also possible that additional studies, if performed and completed, may not be considered sufficient by the FDA to approve any NDA or other application that we submit. If any of these outcomes occur, we may be forced to abandon the development of our product candidates, which would materially adversely affect our business and could potentially cause us to cease operations. We face similar risks for our applications in foreign jurisdictions.

We depend on the successful initiation and completion of clinical trials for RTB101 alone or in combination with everolimus. The positive clinical results, if any, obtained in prior or ongoing clinical trials may not be predictive of future results or repeated in later-stage clinical trials.

Before obtaining regulatory approval for the sale of RTB101, alone or in combination with everolimus, or any other potential product candidate, we must conduct additional clinical trials to demonstrate safety and efficacy in humans. The regulatory requirements for demonstrating efficacy and safety for obtaining approval for reducing the incidence of RTIs or other indications with RTB101 alone or in combination with everolimus may differ. We have not completed the clinical trials necessary to support an application for approval to market RTB101 alone or in combination with everolimus. Successful completion of such clinical trials is a prerequisite to submitting an NDA to the FDA and, consequently, the ultimate approval and commercial marketing of RTB101 alone or in combination with everolimus or any other potential product candidate. A failure of one or more clinical trials can occur at any stage of testing. We need to complete our ongoing Phase 2b clinical trial of RTB101 alone and in combination with everolimus, and subsequently the requisite Phase 3 clinical trials prior to a submission for regulatory approval. We have conducted limited safety studies in humans to date and have only recently commenced our Phase 2b clinical program to assess the safety, tolerability and efficacy of RTB101, alone or in combination with everolimus, in elderly patients. Additional toxicity and metabolism studies may be required by the FDA or other regulatory agencies. A number of companies in the pharmaceutical and biotechnology industries, including those with greater resources and experience than us, have suffered significant setbacks in late stage clinical development, even after seeing promising results in earlier clinical trials.

We may experience a number of unforeseen events during, or as a result of, clinical trials for RTB101, alone or in combination with everolimus, or any other potential product candidate that could adversely affect the costs, timing, or successful completion of our clinical trials, including:

- regulators or other comparable foreign regulatory authorities may disagree as to the design or implementation of our clinical trials;
- regulators, and/or institutional review boards or other reviewing bodies may not authorize us or our investigators to commence a clinical trial, or to conduct or continue a clinical trial at a prospective or specific trial site;
- we may not reach agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;

- clinical trials of RTB101, alone or in combination with everolimus, or any other potential product candidate may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;

- the number of subjects or patients required for clinical trials of RTB101, alone or in combination with everolimus, or any other potential product candidate may be larger than we anticipate, enrollment in these clinical trials may be insufficient or slower than we anticipate, and the number of clinical trials being conducted at any given time may be high and result in fewer available patients for any given clinical trial, or patients may drop out of these clinical trials at a higher rate than we anticipate;

- our third-party contractors, including those manufacturing our product candidates or conducting clinical trials on our behalf, may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;

- we might have to suspend or terminate clinical trials of RTB101, alone or in combination with everolimus, or any other potential product candidate for various reasons, including a finding that the subjects are being exposed to unacceptable health risks;

- we may have to amend clinical trial protocol submitted to regulatory authorities or conduct additional studies to reflect changes in regulatory requirements or guidance, which we may be required to resubmit to an Institutional Review Board, or IRB, and regulatory authorities for re-examination;

- regulators, institutional review boards or data monitoring committees may require or recommend that we or our investigators suspend or terminate clinical research for various reasons, including safety signals or noncompliance with regulatory requirements;

- the cost of clinical trials of RTB101, alone or in combination with everolimus, or any other potential product candidate may be greater than we anticipate;

- regulators, institutional review boards or other reviewing bodies may fail to approve or subsequently find fault with the manufacturing processes or facilities of third-party manufacturers with which we enter into agreement for clinical and commercial supplies, or the supply or quality of RTB101, everolimus or the fixed dose combination of RTB101 and everolimus or any other potential product candidate or other materials necessary to conduct clinical trials of our product candidates may be insufficient, inadequate or not available at an acceptable cost, or we may experience interruptions in supply;

- the potential for approval policies or regulations of the FDA or the applicable foreign regulatory agencies to significantly change in a manner rendering our clinical data insufficient for approval; and

- RTB101, alone or in combination with everolimus, or any other potential product candidate may have undesirable side effects or other unexpected characteristics.

Regulators, institutional review boards of the institutions in which clinical trials are being conducted or data monitoring committees may suspend or terminate a clinical trial due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial.

Negative or inconclusive results from our ongoing clinical trial of RTB101 alone and in combination with everolimus, or any other clinical trial or preclinical studies in animals that we conduct, could mandate repeated or additional clinical trials. We do not know whether any clinical trials that we may conduct will demonstrate adequate efficacy and safety to result in regulatory approval to market RTB101, alone or in combination with everolimus, or any other potential product candidate. If later stage clinical trials do not produce favorable results, our ability to obtain regulatory approval for RTB101, alone or in combination with everolimus, or any other potential product candidate may be adversely impacted.

Clinical trials must be conducted in accordance with the laws and regulations of the FDA, EMA and regulations and other applicable regulatory authorities' legal requirements, regulations or guidelines, and are subject to oversight by these governmental agencies and IRBs at the medical institutions where the clinical trials are conducted. In addition, clinical trials must be conducted with supplies of our product candidates produced under current good manufacturing practice, or cGMP, requirements and other regulations. Furthermore, we rely on CROs, and clinical trial sites to ensure the proper and timely conduct of our clinical trials and while we have agreements governing their committed activities, we have limited influence over their actual performance. We depend on our collaborators and on medical institutions and CROs to conduct our clinical trials in compliance with good clinical practice, or GCP, requirements. To the extent our collaborators or the CROs fail to enroll participants for our clinical trials, fail to conduct the study to GCP standards or are delayed for a significant time in the execution of trials, including achieving full enrollment, we may be affected by increased costs, program delays or both. In addition, clinical trials that are conducted in countries outside the United States and EU may subject us to further delays and expenses as a result of increased shipment costs, additional regulatory requirements and the engagement of non-U.S. and non-EU CROs, as well as expose us to risks associated with clinical investigators who are unknown to the FDA or the EMA, and different standards of diagnosis, screening and medical care.

We may be subject to additional risks because we are administering RTB101 in combination with other mTOR inhibitors, such as everolimus.

We are evaluating RTB101 in combination with other mTOR inhibitors. For example, in our ongoing Phase 2b clinical trial, we are assessing the safety, tolerability and efficacy of RTB101 alone and in combination with everolimus. The use of RTB101 in combination with other compounds may subject us to risks that we would not face if RTB101 were being administered as a monotherapy. For example, the other mTOR inhibitors, including everolimus, may have safety issues that are improperly attributed to RTB101 or the administration of RTB101 with such other therapies may result in safety issues that such other therapies or RTB101 would not have when used alone. In addition, other mTOR inhibitors with which we may administer RTB101, such as everolimus, could be removed from the market and thus be unavailable for testing or commercial use concomitantly with RTB101. The outcome and cost of developing a product candidate to be used with other compounds is difficult to predict and dependent on a number of factors that are outside our reasonable control. If we experience efficacy or safety issues in our clinical trials in which RTB101 is being administered with everolimus, we may not receive regulatory approval for RTB101, which could prevent us from ever generating revenue or achieving profitability.

Competitive products may reduce or eliminate the commercial opportunity for RTB101, alone or in combination with everolimus. If our competitors develop technologies or product candidates more rapidly than we do, or their technologies are more effective or safer than ours, our ability to develop and successfully commercialize RTB101 alone or in combination with everolimus may be adversely affected.

The clinical and commercial landscape for aging-related diseases is highly competitive and subject to rapid and significant technological change. New data from competitors' product candidates continue to emerge. It is possible that these data may alter the current standard of care, completely precluding us from further developing RTB101, alone or in combination with everolimus, for RTIs or other aging-related diseases. Further, it is possible that we may initiate a clinical trial or trials for RTB101, alone or in combination with everolimus, or any other potential product candidate only to find that data from competing products make it impossible for us to complete enrollment in clinical trials, resulting in our inability to submit applications for regulatory approval with regulatory agencies. Even if RTB101 were approved, alone or in combination with everolimus, it may have limited sales due to competition in the specific indications approved.

Competitive therapeutic treatments for aging-related diseases, including RTIs, include those that are currently in development and any new treatments that enter the market. We believe that a significant number of product candidates are currently under development, and may become commercially available in the future, for the treatment of conditions for which we may try to develop product candidates. Our potential competitors include large pharmaceutical and biotechnology companies, specialty pharmaceutical and generic drug companies, academic institutions, government agencies and research institutions. We consider Navitor Pharma to be our most direct competitor in developing novel therapeutics targeting the TORC1 mechanism of action. Additionally, we are also aware of other companies, including Calico and Unity, which are seeking to develop treatments to prevent or treat aging-related diseases through biological pathways that may be unrelated to mTOR inhibition. Similarly, there are several other companies, such as PrEP BioPharm, Virion Health and Innavac, which are pursuing broad-spectrum prophylactic and therapeutic treatments in RTIs.

Many of our competitors have greater financial, technical, manufacturing, marketing, sales and supply resources, and human resources or experience than us and significantly greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of products and the commercialization of those products. Accordingly, our competitors may be more successful than we may be in obtaining regulatory approval for therapies and achieving widespread market acceptance. Our competitors' products may be more effective, or more effectively marketed

and sold, than any product candidate we may commercialize and may render our therapies obsolete or non-competitive before we can recover development and commercialization expenses. If RTB101, alone or in combination with everolimus, is approved for the indications we are currently pursuing, it could compete with a range of therapeutic treatments that are in development. In addition, our competitors may succeed in developing, acquiring or licensing technologies and drug products that are more effective or less costly than RTB101 alone or in combination with everolimus or any other product candidates that we are currently developing or that we may develop, which could render our product candidates obsolete and noncompetitive.

If we obtain approval for RTB101, alone or in combination with everolimus, or any other future product candidate, we may face competition based on many different factors, including the efficacy, safety and tolerability of our products, the ease with which our products can be administered, the timing and scope of regulatory approvals for these products, the availability and cost of manufacturing, marketing and sales capabilities, price, reimbursement coverage and patent position. Existing and future competing products could present superior treatment alternatives, including being more effective, safer, less expensive or marketed and sold more effectively than any products we may develop. Competitive products may make any products we develop obsolete or noncompetitive before we recover the expense of developing and commercializing our product candidates. Such competitors could also recruit our employees, which could negatively impact our level of expertise and our ability to execute our business plan. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a small number of competitors.

We also compete with other clinical stage companies and institutions for clinical trial participants, which could reduce our ability to recruit participants for our clinical trials. Delay in recruiting clinical trial participants could adversely affect our ability to bring a product to market prior to our competitors. Further, research and discoveries by others may result in breakthroughs that render our product candidates obsolete even before they begin to generate any revenue.

In addition, our competitors may obtain patent protection, regulatory exclusivities, or FDA approval and commercialize products more rapidly than we do, which may impact future approvals or sales of any of our product candidates that receive regulatory approval. If the FDA approves the commercial sale of RTB101, alone or in combination with everolimus, or any other product candidate, we will also be competing with respect to marketing capabilities and manufacturing efficiency. We expect competition among products will be based on product efficacy and safety, the timing and scope of regulatory approvals, availability of supply, marketing and sales capabilities, product price, reimbursement coverage by government and private third-party payers, regulatory exclusivities and patent position. Our profitability and financial position will suffer if our product candidates receive regulatory approval, but cannot compete effectively in the marketplace.

Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical trial sites, as well as in acquiring technologies complementary to, or necessary for, our programs.

Furthermore, regulatory authorities' assessment of the data and results required to demonstrate safety and efficacy can change over time and can be affected by many factors, such as the emergence of new information, including on other products, changing policies and agency funding, staffing and leadership. We cannot be sure whether future changes to the regulatory environment will be favorable or unfavorable to our business prospects. For example, average review times at the FDA for regulatory approval applications can be affected by a variety of factors, including budget and funding levels and statutory, regulatory and policy changes.

The regulatory approval processes of the FDA, EMA and comparable foreign authorities are lengthy, time consuming and inherently unpredictable. If clinical trials of RTB101, alone or in combination with everolimus, fail to satisfactorily demonstrate safety and efficacy to the FDA or other regulators, or do not otherwise produce favorable results, we, or any future collaborators, may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of RTB101 alone or in combination with everolimus.

We, and any future collaborators, are not permitted to commercialize, market, promote or sell any product candidate in the United States without obtaining regulatory approval from the FDA. Foreign regulatory authorities, such as the EMA, impose similar requirements. The time required to obtain approval by the FDA, EMA and comparable foreign authorities is unpredictable, but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or

the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. To date, we have not submitted an NDA to the FDA or similar drug approval submissions to comparable foreign regulatory authorities for RTB101, alone or in combination with everolimus, or any other product candidate. We, and any future collaborators, must complete additional preclinical or nonclinical studies and clinical trials to demonstrate the safety and efficacy of our product candidates in humans before we will be able to obtain these approvals.

Clinical testing is expensive, difficult to design and implement, can take many years to complete and is inherently uncertain as to outcome. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, if at all. The clinical development of RTB101 alone or in combination with everolimus or other drugs is susceptible to the risk of failure inherent at any stage of development, including failure to demonstrate efficacy in a clinical trial or across a broad population of patients, the occurrence of adverse events that are severe or medically or commercially unacceptable, failure to comply with protocols or applicable regulatory requirements, and determination by the FDA or any comparable foreign regulatory authority that a product candidate may not continue development or is not approvable. It is possible that even if RTB101, alone or in combination with everolimus, or any other product candidate has a beneficial effect, that effect will not be detected during clinical evaluation as a result of one or more of a variety of factors, including the seasonal and geographical RTI rates and size, duration, design, measurements, conduct or analysis of our clinical trials. Conversely, as a result of the same factors, our clinical trials may indicate an apparent positive effect of RTB101, alone or in combination with everolimus, or any other product candidate that is greater than the actual positive effect, if any. Similarly, in our clinical trials we may fail to detect toxicity of or intolerability caused by RTB101, everolimus or any other product candidate, or mistakenly believe that our product candidates are toxic or not well tolerated when that is not in fact the case.

Any inability to successfully complete preclinical and clinical development could result in additional costs to us, or any future collaborators. Moreover, if we, or any future collaborators, are required to conduct additional clinical trials or other testing of RTB101, alone or in combination with everolimus, or any other product candidate beyond the trials and testing that we or they contemplate, if we or they are unable to successfully complete clinical trials of our product candidates or other testing or the results of these trials or tests are unfavorable, uncertain or are only modestly favorable, or there are unacceptable safety concerns associated with our product candidates, we, or any future collaborators may:

- incur additional unplanned costs;
- be delayed in obtaining regulatory approval for our product candidates;
- not obtain regulatory approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or significant safety warnings, including boxed warnings;
- be subject to additional post-marketing testing or other requirements; or
- be required to remove the product from the market after obtaining regulatory approval.

Our failure to successfully initiate and complete clinical trials of RTB101, alone or in combination with everolimus, or any other product candidate and to demonstrate the efficacy and safety necessary to obtain regulatory approval to market RTB101, alone or in combination with everolimus, or any other product candidate would significantly harm our business. Our product candidate development costs will also increase if we experience delays in testing or regulatory approvals and we may be required to obtain additional funds to complete clinical trials. We cannot assure you that our clinical trials will begin as planned or be completed on schedule, if at all, or that we will not need to restructure our trials after they have begun. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates, which may harm our business and results of operations. In addition, many of the factors that cause, or lead to, delays of clinical trials may ultimately lead to the denial of regulatory approval of RTB101 alone or in combination with everolimus or any other product candidate.

Our product candidates 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 regulatory approval, if obtained.

Undesirable side effects caused by RTB101, alone or in combination with everolimus, or any other product candidate could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or comparable foreign regulatory authorities. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. In clinical trials of RTB101, alone or in combination with everolimus, to date, there were no observed study drug-related serious adverse events in the Phase 2a clinical trial except in the placebo arm. The majority of observed study-drug related adverse events were mild or moderate in severity, transient and resolved without stopping the study drug. However, there can be no guarantee that we would observe a similar tolerability profile of RTB101, alone or in combination with everolimus, in our ongoing Phase 2b clinical trial or in future clinical trials. Many compounds that initially showed promise in clinical or earlier stage testing are later found to cause undesirable or unexpected side effects that prevented further development of the compound.

If unacceptable side effects arise in the development of our product candidates, we, the FDA or comparable foreign regulatory authorities, the IRBs, or independent ethics committees at the institutions in which our trials are conducted, or the Data Safety Monitoring Board, or DSMB, could suspend or terminate our clinical trials or the FDA or comparable foreign regulatory authorities could order us to cease clinical trials or deny approval of our product candidates for any or all targeted indications. Treatment-emergent side effects that are deemed to be treatment-related could also affect subject recruitment or the ability of enrolled subjects to complete the trial or result in potential product liability claims. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff. We expect to have to train medical personnel using our product candidates to understand the side effect profiles for our clinical trials and upon any commercialization of any of our product candidates. Inadequate training in recognizing or managing the potential side effects of our product candidates could result in patient injury or death. Any of these occurrences may harm our business, financial condition and prospects significantly.

Moreover, clinical trials of our product candidates are conducted in carefully defined sets of patients who have agreed to enter into clinical trials. Consequently, it is possible that our clinical trials, or those of any future collaborator, may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any, or alternatively fail to identify undesirable side effects. If, following approval of a product candidate, we, or others, discover that the product is less effective than previously believed or causes undesirable side effects that were not previously identified, any of the following adverse consequences could occur:

- regulatory authorities may withdraw their approval of the product, seize the product, or seek an injunction against its manufacture or distribution;
- we, or any future collaborators, may need to recall the product, or be required to change the way the product is administered or conduct additional clinical trials, develop a surveillance program;
- additional restrictions may be imposed on the marketing of, or the manufacturing processes for, the particular product;
- regulatory authorities may require one or more post-market studies;
- we may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- regulatory authorities may require the addition of labeling statements, such as a “black box” warning or a contraindication, or issue safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings or other safety information about the product;
- we, or any future collaborators, may be required to create a Medication Guide outlining the risks of the previously unidentified side effects for distribution to patients;
- we, or any future collaborators, could be sued and held liable for harm caused to patients;

- the product may become less competitive; and
- our reputation may suffer.

Any of these events could harm our business and operations, and could negatively impact our stock price.

If we fail to develop and commercialize RTB101, alone or in combination with everolimus, for additional indications or fail to discover, develop and commercialize other product candidates, we may be unable to grow our business and our ability to achieve our strategic objectives would be impaired.

Although the development and commercialization of RTB101 alone or in combination with everolimus for RTIs is our primary focus, as part of our longer-term growth strategy, we may evaluate RTB101, alone or in combination with everolimus, in other indications and develop other product candidates. We intend to evaluate internal opportunities from RTB101, alone or in combination with everolimus, or other product candidates from our TORC1 program, and also may choose to in-license or acquire other product candidates as well as commercial products to treat patients suffering from other disorders with significant unmet medical needs and limited treatment options. These other product candidates will require additional, time-consuming development efforts prior to commercial sale, including preclinical studies, clinical trials and approval by the FDA and/or applicable foreign regulatory authorities. All product candidates are prone to the risks of failure that are inherent in pharmaceutical product development, including the possibility that the product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities. In addition, we cannot assure you that any such products that are approved will be manufactured or produced economically, successfully commercialized or widely accepted in the marketplace or be more effective than other commercially available alternatives.

Research programs to identify product candidates require substantial technical, financial and human resources, whether or not any product candidates are ultimately identified. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for many reasons, including the following:

- the research methodology used may not be successful in identifying potential product candidates;
- competitors may develop alternatives that render our product candidates obsolete;
- product candidates that we develop may nevertheless be covered by third parties' patents or other exclusive rights;
- a product candidate may, on further study, be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all; and
- a product candidate may not be accepted as safe and effective by patients, the medical community or third-party payors.

If we are unsuccessful in identifying and developing additional product candidates, our potential for growth and achieving our strategic objectives may be impaired.

Our preclinical programs may not produce new product candidates that are suitable for clinical trials or that can be successfully commercialized or generate revenue through collaborations.

We must successfully complete preclinical testing for our preclinical programs, including our TORC1 follow-on program, which may include demonstrating activity and comprehensive studies to show the lack of toxicity and other adverse effects in established animal models, before commencing clinical trials for any product candidate. Many pharmaceutical products do not successfully complete preclinical testing and, even if preclinical testing is successfully completed, may fail in clinical trials. In addition, there can be no assurance that positive results from preclinical studies will be predictive of results obtained from subsequent preclinical studies or clinical trials. Many pharmaceutical candidates are not suitable for manufacture on the scale or of the quality required for clinical trials or commercialization. Some pharmaceutical candidates

that initially seem suitable may later be found to be insufficiently stable or may generate toxic impurities over time. We also cannot be certain that any product candidates that do advance into clinical trials will successfully demonstrate safety and efficacy in clinical trials. Even if we achieve positive results in early preclinical studies or clinical trials, they may not be predictive of the results in later trials.

We may expend our resources to pursue a particular product candidate or indication and forgo the opportunity to capitalize on product candidates or indications that may ultimately be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we intend to focus on developing product candidates for specific indications that we identify as most likely to succeed, in terms of both their potential for regulatory approval and commercialization. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that may prove to have greater commercial potential.

Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable product candidates. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to the product candidate.

If the FDA or comparable foreign regulatory authorities approve generic versions of RTB101, alone or in combination with everolimus, or any other product candidate of ours that receives regulatory approval, or such authorities do not grant our products appropriate periods of non-patent exclusivity before approving generic versions of such products, the sales of such products could be adversely affected.

Once an NDA is approved, the product covered thereby becomes a "listed drug" in the FDA's publication, "Approved Drug Products with Therapeutic Equivalence Evaluations," or the Orange Book. Manufacturers may seek approval of generic versions of reference listed drugs through submission of abbreviated new drug applications, or ANDAs, in the United States. In support of an ANDA, a generic manufacturer generally must show that its product has the same active ingredient(s), dosage form, strength, route of administration, conditions of use and labeling as the reference listed drug and that the generic version is bioequivalent to the reference listed drug, meaning, in part, that it is absorbed in the body at the same rate and to the same extent. Generic products may be significantly less costly to bring to market than the reference listed drug and companies that produce generic products are generally able to offer them at lower prices. Moreover, many states allow or require substitution of therapeutically equivalent generic drugs at the pharmacy level even if the branded drug is prescribed. Thus, following the introduction of a generic drug, a significant percentage of the sales of any branded product or reference listed drug may be lost to the generic product.

The FDA may not approve an ANDA for a generic product until any applicable period of non-patent exclusivity for the reference listed drug has expired. The Federal Food, Drug, and Cosmetic Act, or FDCA, provides a period of five years of non-patent exclusivity for a new drug containing a new chemical entity, or NCE. Specifically, in cases where such exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification that a patent covering the listed drug is invalid, unenforceable or will not be infringed by the generic product, in which case the applicant may submit its application four years following approval of the listed drug. It is unclear whether the FDA will treat the active ingredients in our product candidates as NCEs and, therefore, afford them five years of NCE data exclusivity if they are approved. If any product we develop does not receive five years of NCE exclusivity, the FDA may approve generic versions of such product three years after its date of approval, subject to the requirement that the ANDA applicant certifies to any patents listed for our products in the Orange Book. Three year exclusivity is given to a drug if it contains an active moiety that has previously been approved, and the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the NDA. If approved, manufacturers may seek to launch these generic products following the expiration of the applicable marketing exclusivity period, even if we still have patent protection for our product.

Competition that our products, if approved, may face from generic versions of our products could negatively impact our future revenue, profitability and cash flows and substantially limit our ability to obtain a return on our investments in those product candidates.

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

We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons. The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the study until its conclusion.

Patient enrollment is affected by many factors, including:

- the patient eligibility criteria defined in the protocol;
- the size of the patient population required for analysis of the trial's primary endpoints;
- the proximity of patients to study sites;
- the design of the trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- competing clinical trials and clinicians' and patients' perceptions as to the potential advantages and risks of the product candidate being studied in relation to other available therapies, including any new drugs that may be approved for the indications that we are investigating;
- our ability to obtain and maintain patient consents; and
- the risk that patients enrolled in clinical trials will drop out of the trials before completion.

In addition, our clinical trials will compete with other clinical trials for product candidates that are in the same therapeutic areas as our product candidates, and this competition will reduce the number and types of patients available to us, because some patients who might have opted to enroll in our trials may instead opt to enroll in a trial being conducted by one of our competitors. Since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials in such clinical trial site. In addition, because we intend to investigate our product candidates during the winter cold and flu season, this timing requirement may further limit the available pool of clinical trial subjects.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or might require us to abandon one or more clinical trials altogether. Delays in patient enrollment may result in increased costs, affect the timing or outcome of the planned clinical trials, product candidate development and approval process and jeopardize our ability to seek and obtain the regulatory approval required to commence product sales and generate revenue, which could prevent completion of these trials, adversely affect our ability to advance the development of our product candidates, cause the value of our company to decline and limit our ability to obtain additional financing if needed.

Ingredients, excipients and other materials necessary to manufacture RTB101 or everolimus may not be available on commercially reasonable terms, or at all, which may adversely affect the development and commercialization of RTB101, alone or in combination with everolimus.

We and our third-party manufacturers must obtain from other third-party suppliers the active pharmaceutical ingredients, excipients and primary and secondary packaging materials necessary for our contract manufacturers to produce RTB101 or everolimus for our clinical trials and, to the extent approved or commercialized, for commercial distribution. There is no guarantee that we would be able to enter into all the necessary agreements with third-party suppliers that we require for the supply of such materials on commercially reasonable terms or at all. Even if we were able to secure such agreements or guarantees, our suppliers may be unable or choose not to provide us the ingredients, excipients or materials in a timely manner or in the quantities required. If we or our third-party manufacturers are unable to obtain the quantities of these ingredients, excipients or materials that are necessary for the manufacture of commercial supplies of RTB101 or everolimus, our ability to generate revenue from the sale of RTB101 alone or in combination with everolimus would be materially and adversely affected. Further, if we or our third-party manufacturers are unable to obtain active pharmaceutical ingredients, excipients and materials as necessary for our clinical trials or for the manufacture of commercial supplies of our product candidates, if approved, potential regulatory approval or commercialization would be delayed, which would materially and adversely affect our ability to generate revenue from the sale of our product candidates. As a result of these and other factors, the cost of manufacturing drug material may not support continued development or commercialization or may materially reduce revenue.

Even if RTB101, alone or in combination with everolimus, or any other product candidate of ours receives regulatory approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success, in which case we may not generate significant revenues or become profitable.

We have never commercialized a product, and even if RTB101, alone or in combination with everolimus, or any other 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. The market for therapies targeting aging-related diseases with an immunotherapy is novel, and physicians may be reluctant to adopt novel therapies. In addition, patients and their physicians may not desire to add RTB101, alone or in combination with everolimus, even if approved, to their existing prophylactic treatment regime. For example, physicians are often reluctant to switch their patients from existing prophylactics for RTIs even when new and potentially more effective or convenient alternatives enter the market. 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 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 RTB101, alone or in combination with everolimus, or any other product candidate is approved but does 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 recommended under physician prophylactic guidelines;
- 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.

Any failure by RTB101 alone or in combination with everolimus or any other product candidate of ours that obtains regulatory approval to achieve market acceptance or commercial success would adversely affect our business prospects.

Even if we, or any future collaborators, are able to commercialize any product candidate that we, or they, develop, the product may become subject to unfavorable pricing regulations or third-party payor coverage and reimbursement policies, any of which could harm our business.

Patients who are provided medical treatment for their conditions generally rely on third party payors to reimburse all or part of the costs associated with their treatment. Therefore, our ability, and the ability of any future collaborators to commercialize any of our product candidates will depend in part on the extent to which coverage and reimbursement for these products and related treatments will be available from third-party payors including government health administration authorities and private health coverage insurers. Third-party payors decide which medications they will cover and establish reimbursement levels. We cannot be certain that coverage will be available and reimbursement will be adequate for RTB101, alone or in combination with everolimus, or any of our other product candidates. Also, we cannot be certain that reimbursement policies will not reduce the demand for, or the price paid for, our products.

If coverage and reimbursement are not available, or reimbursement is available only to limited levels, we, or any future collaborators, may be limited in our ability to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us, or any future collaborators, to establish or maintain pricing sufficient to realize a sufficient return on our or their investment. In the United States, no uniform policy of coverage and reimbursement for products exists among third-party payors and coverage and reimbursement for products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

There is significant uncertainty related to third-party payor coverage and reimbursement of newly approved drugs. Regulatory approvals, pricing and reimbursement for new drug products vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we, or any future collaborators, might obtain regulatory approval for a product in a particular country, but then be subject to price regulations that delay commercial launch of the product, which may negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability or the ability of any future collaborators to recoup our or their investment in one or more product candidates, even if our product candidates obtain regulatory approval.

The healthcare industry is acutely focused on cost containment, both in the United States and elsewhere. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for certain medications, which could affect our ability or that of any future collaborators to sell our product candidates profitably. These payors may not view our products, if any, as cost-effective, and coverage and reimbursement may not be available to our customers, or those of any future collaborators, or may not be sufficient to allow our products, if any, to be marketed on a competitive basis. Cost-control initiatives could cause us, or any future collaborators, to decrease the price we, or they, might establish for products, which could result in lower than anticipated product revenues. If the prices for our products, if any, decrease or if governmental and other third-party payors do not provide coverage or adequate reimbursement, our prospects for revenue and profitability will suffer.

There may also be delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the indications for which the drug is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Reimbursement rates may vary, by way of example, according to the use of the product and the clinical setting in which it is used. Reimbursement rates may also be based on reimbursement levels already set for lower cost drugs or may be incorporated into existing payments for other services.

In addition, increasingly, third-party payors are requiring higher levels of evidence of the benefits and clinical outcomes of new technologies and are challenging prices. We cannot be sure that coverage will be available for any product candidate that we, or any future collaborator, commercialize and, if available, that the reimbursement rates will be adequate. Further, the net reimbursement for drug products may be subject to additional reductions if there are changes to laws that presently restrict imports of drugs from one country to another. An inability to promptly obtain coverage and adequate payment rates from both government-funded and private payors for any of our product candidates for which we, or any future collaborator, obtain regulatory approval could significantly harm our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Product liability lawsuits against us or any of our future collaborators could divert our resources and attention, cause us to incur substantial liabilities and limit commercialization of our product candidates.

We are exposed to potential product liability and professional indemnity risks that are inherent in the research, development, manufacturing, marketing and use of pharmaceutical products. Currently, we have no products that have been approved for commercial sale; however, the current and future use of our product candidates by us and any collaborators in clinical trials, and the sale of these product candidates, if approved, in the future, may expose us to liability claims. We face an inherent risk of product liability lawsuits related to the use of our product candidates in elderly patients and will face an even greater risk if product candidates are approved by regulatory authorities and introduced commercially. Product liability claims may be brought against us or our partners by participants enrolled in our clinical trials, patients, health care providers, pharmaceutical companies, our collaborators or others using, administering or selling any of our future approved products. If we cannot successfully defend ourselves against any such claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for any of our future approved products;
- injury to our reputation;
- withdrawal of clinical trial participants;
- termination of clinical trial sites or entire trial programs;
- significant litigation costs;
- substantial monetary awards to, or costly settlements with, patients or other claimants;
- product recalls or a change in the indications for which they may be used;
- loss of revenue;
- diversion of management and scientific resources from our business operations; and
- the inability to commercialize our product candidates.

Although the clinical trial process is designed to identify and assess potential side effects, clinical development does not always fully characterize the safety and efficacy profile of a new medicine, and it is always possible that a drug, even after regulatory approval, may exhibit unforeseen side effects. If our product candidates were to cause adverse side effects during clinical trials or after approval, we may be exposed to substantial liabilities. Physicians and patients may not comply with any warnings that identify known potential adverse effects and patients who should not use our product candidates. If any of our product candidates are approved for commercial sale, we will be highly dependent upon consumer perceptions of us and the safety and quality of our products. We could be adversely affected if we are subject to negative publicity associated with illness or other adverse effects resulting from patients' use or misuse of our products or any similar products distributed by other companies.

Although we maintain product liability insurance coverage in the amount of up to $10.0 million in the aggregate, including clinical trial liability, this insurance may not fully cover potential liabilities that we may incur. The cost of any product liability litigation or other proceeding, even if resolved in our favor, could be substantial. We will need to increase our insurance coverage if we commercialize any product that receives regulatory approval. In addition, insurance coverage is becoming increasingly expensive. If we are unable to maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product liability claims, it could prevent or inhibit the development and commercial production and sale of our product candidates, which could harm our business, financial condition, results of operations and prospects.

We currently have no marketing, sales or distribution infrastructure. If we are unable to develop our sales, marketing and distribution capability on our own or through collaborations with marketing partners, we will not be successful in commercializing our product candidates.

We currently have no marketing, sales or distribution capabilities. If RTB101, alone or in combination with everolimus, is approved for RTIs, we intend to establish a sales and marketing organization with technical expertise and supporting distribution capabilities to commercialize the approved product in key territories, which will require substantial additional resources. Some or all of these costs may be incurred in advance of any approval of RTB101, alone or in combination with everolimus. Any failure or delay in the development of our or third parties' internal sales, marketing and distribution capabilities would adversely impact the commercialization of RTB101, alone or in combination with everolimus, and other future product candidates.

Factors that may inhibit our efforts to commercialize our products on our own include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to or persuade adequate numbers of physicians to prescribe any future products;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

With respect to our existing and future product candidates, we may choose to collaborate with third parties that have direct sales forces and established distribution systems to serve as an alternative to our own sales force and distribution systems. Our product revenue may be lower than if we directly marketed or sold our products, if approved. In addition, any revenue we receive will depend in whole or in part upon the efforts of these third parties, which may not be successful and are generally not within our control. If we are not successful in commercializing any approved products, our future product revenue will suffer and we may incur significant additional losses.

If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

If we, or any future collaborators, experience any of a number of possible unforeseen events in connection with clinical trials of RTB101, alone or in combination with everolimus, or any other product candidate, potential clinical development, regulatory approval or commercialization of our product candidates could be delayed or prevented.

We, or any future collaborators, may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent clinical development, regulatory approval or commercialization of our product candidates, including:

- our product candidates may produce unfavorable or inconclusive results;
- regulators may require us or any future collaborators, to conduct additional clinical trials or abandon product development programs;
- the number of patients required for clinical trials of our product candidates may be larger than we, or any future collaborators anticipate, patient enrollment in these clinical trials may be slower than we, or any future collaborators, may anticipate or participants may drop out of these clinical trials at a higher rate than we, or any future collaborators, anticipate;
- the cost of planned clinical trials of our product candidates may be greater than we anticipate;
- our third-party contractors or those of any future collaborators, including those manufacturing our product candidates or components or ingredients thereof or conducting clinical trials on our behalf or on behalf of any future collaborators, may fail to comply with regulatory requirements or meet their contractual obligations to us or any future collaborators in a timely manner or at all;

- regulators, IRBs or independent ethics committees may not authorize us, any future collaborators or our or their investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;

- delays in reaching or failure to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;

- patients who enroll in a clinical trial may misrepresent their eligibility to do so or may otherwise not comply with the clinical trial protocol, resulting in the need to drop the patients from the clinical trial, increase the needed enrollment size for the clinical trial or extend the clinical trial's duration;

- delay, suspension or termination of clinical trials of our product candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate; and

- regulators, IRBs or independent ethics committees may require that we, or any future collaborators, or our or their investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or their standards of conduct, a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate or findings of undesirable effects caused by a chemically or mechanistically similar product or product candidate.

Further, conducting clinical trials in foreign countries, as we have done and plan to do for our product candidates, presents additional risks that may delay completion of our clinical trials. These risks include the failure of enrolled patients in foreign countries to adhere to clinical protocol as a result of differences in healthcare services or cultural customs, managing additional administrative burdens associated with foreign regulatory schemes, as well as political and economic risks relevant to such foreign countries.

Product development costs for us, or any future collaborators, will increase if we, or they, experience delays in testing or pursuing regulatory approvals and we, or they, may be required to obtain additional funds to complete clinical trials and prepare for possible commercialization of our product candidates. We do not know whether any preclinical studies or clinical trials will begin as planned, will need to be restructured, or will be completed on schedule or at all. Significant preclinical study or clinical trial delays also could shorten any periods during which we, or any future collaborators, may have the exclusive right to commercialize our product candidates or allow our competitors, or the competitors of any future collaborators, to bring products to market before we, or any future collaborators, do and impair our ability, or the ability of any future collaborators, to successfully commercialize our product candidates and may harm our business and results of operations. In addition, many of the factors that lead to clinical trial delays may ultimately lead to the denial of regulatory approval of any of our product candidates.

Results of preclinical studies and early clinical trials may not be predictive of results of future clinical trials, and such results do not guarantee approval of a product candidate by regulatory authorities.

The outcome of preclinical studies and early clinical trials may not be predictive of the success of later clinical trials, and interim results of clinical trials do not necessarily predict success in the results of completed clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in earlier development, and we could face similar setbacks. The design of a clinical trial can determine whether its results will support approval of a product and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. In addition, preclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain regulatory approval for their product candidates. Even if we complete clinical development of RTB101 alone or in combination with everolimus for RTIs or any other indication, there can be no assurance that the FDA, EMA, or other regulatory authorities will approve RTB101 alone or in combination with everolimus for marketing.

In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the dosing regimen and other clinical trial procedures and the rate of dropout among clinical trial participants. If we fail to receive positive results in clinical trials of our product candidates, the development timeline and regulatory approval and commercialization prospects for our most advanced product candidate, and, correspondingly, our business and financial prospects would be negatively impacted.

Risks Related to Regulatory Approval and Marketing of Our Product Candidates and Other Legal Compliance Matters

Even if we complete the necessary preclinical studies and clinical trials, the regulatory approval process for product candidates is expensive, time consuming and uncertain and may prevent us or any future collaborators from obtaining approvals for the commercialization of RTB101 alone or in combination with everolimus or any other product candidate. As a result, we cannot predict when or if, and in which territories, we, or any future collaborators, will obtain regulatory approval to commercialize a product candidate.

The research, testing, manufacturing, labeling, approval, selling, marketing, promotion and distribution of products are subject to extensive regulation by the FDA and comparable foreign regulatory authorities. We, and any future collaborators, are not permitted to market RTB101, alone or in combination with everolimus, or any other product candidate in the United States or in other countries until we, or they, receive approval of an NDA from the FDA or regulatory approval from applicable regulatory authorities outside the United States. RTB101 is in clinical development and is subject to the risks of failure inherent in drug development. We have not submitted an application for or received regulatory approval for RTB101, alone or in combination with everolimus, or any other product candidate in the United States or in any other jurisdiction. We have limited experience in conducting and managing the clinical trials necessary to obtain regulatory approvals, including obtaining FDA approval of an NDA.

The process of obtaining regulatory approvals, both in the United States and abroad, is lengthy, expensive and uncertain. It may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Securing regulatory approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing regulatory approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. The FDA or other regulatory authorities may determine that RTB101, alone or in combination with everolimus, or any other product candidates are not safe and effective, only moderately effective or have undesirable or unintended side effects, toxicities or other characteristics that preclude our obtaining regulatory approval or prevent or limit commercial use. Any regulatory approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

In addition, changes in regulatory approval policies during the development period, changes in or the enactment or promulgation of additional statutes, regulations or guidance or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent regulatory approval of a product candidate. Any regulatory approval we, or any future collaborators, ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or other regulatory authority. The FDA or other regulatory authority may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA or other regulatory authority may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA or other regulatory authority, as the case may be, and may ultimately lead to the denial of regulatory approval of one or more of our product candidates.

Any delay in obtaining or failure to obtain required approvals could negatively impact our ability or that of any future collaborators to generate revenue from the particular product candidate, which likely would result in significant harm to our business and adversely impact our stock price.

Our failure to obtain regulatory approval in foreign jurisdictions would prevent our product candidates from being marketed abroad, and any approval we are granted for RTB101, alone or in combination with everolimus, or any of our other product candidates in the United States would not assure approval of product candidates in foreign jurisdictions.

In order to market any products outside of the United States, we must establish and comply with numerous and varying regulatory requirements of other countries regarding clinical trial design, safety and efficacy. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries, and regulatory approval in one country does not mean that regulatory approval will be obtained in any other country. Approval procedures vary among countries and can involve additional product testing and validation and additional administrative review periods. Seeking foreign regulatory approvals could result in significant delays, difficulties and costs for us and may require additional preclinical studies or clinical trials which would be costly and time consuming and could delay or prevent introduction of RTB101, alone or in combination with everolimus, or any of our other product candidates in those countries. We do not have experience in obtaining regulatory approval in international markets. If we or our partners fail to comply with regulatory requirements or to obtain and maintain required approvals, our target market will be reduced and our ability to realize the full market potential of our product candidates will be harmed.

Additionally, on June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. On March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. Since a significant proportion of the regulatory framework in the United Kingdom is derived from European Union directives and regulations, the referendum could materially impact the regulatory regime with respect to the approval of our product candidates in the United Kingdom or the European Union. Any delay in obtaining, or an inability to obtain, any regulatory approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom and/or the European Union and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or European Union for our product candidates, which could significantly and materially harm our business.

Even if we, or any future collaborators, obtain regulatory approvals for our product candidates, the terms of approvals and ongoing regulation of our products may limit how we manufacture and market our products, which could impair our ability to generate revenue.

Once regulatory approval has been granted, an approved product and its manufacturer and marketer are subject to ongoing review and extensive regulation. We, and any future collaborators, must therefore comply with requirements concerning advertising and promotion for any of our product candidates for which we or they obtain regulatory approval. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved labeling. Thus, we and any future collaborators will not be able to promote any products we develop for indications or uses for which they are not approved.

In addition, manufacturers of approved products and those manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to current Good Manufacturing Practices, or cGMPs, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We, our contract manufacturers, any future collaborators and their contract manufacturers could be subject to periodic unannounced inspections by the FDA to monitor and ensure compliance with cGMPs. Despite our efforts to inspect and verify regulatory compliance, one or more of our third-party manufacturing vendors may be found on regulatory inspection by FDA or other authorities to be not in compliance with cGMP regulations, which may result in shutdown of the third-party vendor or invalidation of drug product lots or processes. In some cases, a product recall may be warranted or required, which would materially affect our ability to supply and market our drug products.

Accordingly, assuming we, or any future collaborators, receive regulatory approval for one or more of our product candidates, we, and any future collaborators, and our and their contract manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control.

If we, and any future collaborators, are not able to comply with post-approval regulatory requirements, we, and any future collaborators, could have the regulatory approvals for our products withdrawn by regulatory authorities and our, or any future collaborators', ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

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

Both before and after approval of any product, we and our 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 trials, 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 product recall; product seizure; interruption of manufacturing or clinical trials; 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.

Obtaining FDA approval of our product candidates requires substantial time, effort and financial resources and may be subject to both expected and unforeseen delays, and there can be no assurance that any approval will be granted for any of our product candidates on a timely basis, if at all. The FDA may decide that our data are insufficient for approval of our product candidates and require additional preclinical, clinical or other studies or additional work related to chemistry, manufacturing and controls. In addition, we, the FDA, IRBs or independent ethics committees may suspend or terminate human clinical trials at any time on various grounds, including a finding that the patients are or would be exposed to an unacceptable health risk or because of the way in which the investigators on which we rely carry out the trials. If we are required to conduct additional trials or to conduct other testing of our product candidates beyond that which we currently contemplate for regulatory approval, if we are unable to complete successfully our clinical trials or other testing, or if the results of these and other trials or tests fail to demonstrate efficacy or raise safety concerns, we may face substantial additional expenses, be delayed in obtaining regulatory approval for our product candidates or may never obtain regulatory approval.

We are also required to comply with extensive governmental regulatory requirements after a product has received marketing authorization. Governing regulatory authorities may require post-marketing studies that may negatively impact the commercial viability of a product. Once on the market, a product may become associated with previously undetected adverse effects and/or may experience manufacturing or other commercial difficulties. As a result of any of these or other problems, a product's regulatory approval could be withdrawn, which could harm our business and operating results.

Any of our product candidates for which we, or any future collaborators, obtain regulatory approval in the future will be subject to 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 future 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.

Any of our product candidates for which we, or any future collaborators, obtain regulatory approval, as well as the manufacturing processes, post-approval studies, labeling, advertising and promotional activities for such product, among other things, will be subject to ongoing requirements of and review by the FDA, EMA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. We and our contract manufacturers will also be subject to user fees and periodic inspection by the FDA, EMA and other regulatory authorities to monitor compliance with these requirements and the terms of any product approval we may obtain. Even if regulatory approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, including the requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS.

The FDA, EMA and other regulatory authorities may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of a product. The FDA and other agencies, including the Department of Justice, closely regulate and monitor the post-approval marketing and promotion of products to ensure that they are manufactured, marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and if we, or any future collaborators, do not market any of our product candidates for which we, or they, receive regulatory

approval for only their approved indications, we, or they, may be subject to warnings or enforcement action for off-label marketing if it is alleged that we are doing so. Violation of the FDCA and other statutes relating to the promotion and advertising of prescription drugs may lead to investigations or allegations of violations of federal and state health care fraud and abuse laws and state consumer protection laws, including the False Claims Act.

In addition, later discovery of previously unknown adverse events or other problems with our products or their manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on the manufacturing of such products;
- restrictions on the labeling or marketing of such products;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- restrictions on coverage by third-party payors;
- fines, restitution or disgorgement of profits or revenues;
- exclusion from federal health care programs such as Medicare and Medicaid;
- suspension or withdrawal of regulatory approvals;
- refusal to permit the import or export of products;
- product seizure; or
- injunctions or the imposition of civil or criminal penalties.

The efforts of the Administration to pursue regulatory reform may limit FDA's ability to engage in oversight and implementation activities in the normal course, and that could negatively impact our business.

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 Trump administration may impact our business and industry. Namely, the Trump 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, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. On January 30, 2017, President Trump issued an executive order, applicable to all executive agencies, including the FDA, that requires that for each notice of proposed rulemaking or final regulation to be issued in fiscal year 2017, the agency shall identify at least two existing regulations to be repealed, unless prohibited by law. These requirements are referred to as the "two-for-one" provisions. This executive order includes a budget neutrality provision that requires the total incremental cost of all new regulations in the 2017 fiscal year, including repealed regulations, to be no greater than zero, except in limited circumstances. For fiscal years 2018 and beyond, the executive order requires agencies to identify regulations to offset any incremental cost of a new regulation. In interim guidance issued by the Office of Information and Regulatory Affairs within OMB on February 2, 2017, the administration indicates that the "two-

for-one" provisions may apply not only to agency regulations, but also to significant agency guidance documents, and 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 these Executive Orders. 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 constraints on FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

Our relationships with healthcare providers, physicians and third-party payors will be subject to applicable anti-kickback, fraud and abuse, privacy and transparency and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, exclusion from government healthcare programs, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any products for which we obtain regulatory approval. Our future arrangements with third party payors, healthcare providers and physicians may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we conduct our operations, including how we research, market, sell and distribute any products for which we obtain regulatory approval. These include the following:

- **Anti-Kickback Statute**—The federal healthcare anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation or arranging of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid. A person or entity can be found guilty of violating the federal Anti-Kickback Statute without actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act or federal civil money penalties statute;

- **False Claims Act**—The federal False Claims Act imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented false or fraudulent claims for payment by a federal healthcare program; making a false statement or record material to a false or fraudulent claim or an obligation to pay money to the federal government; or avoiding, decreasing or concealing an obligation to pay money to the federal government. A claim that includes items or services resulting from a violation of the Anti-Kickback Statute constitutes a false or fraudulent claim under the False Claims Act. Potential liability for violating the False Claims Act includes mandatory treble damages and significant per-claim penalties;

- **HIPAA**—The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters. Similar to the Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, HIPAA and, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations on covered entities and their business associates, including mandatory contractual terms and technical safeguards, with respect to maintaining the privacy, security and transmission of individually identifiable health information;

- **Transparency Requirements**—Federal laws require applicable manufacturers of covered drugs to report payments and other transfers of value to physicians, including doctors, dentists, optometrists, podiatrists and chiropractors, and teaching hospitals, as well as information regarding ownership and investment interests held by the physicians described above and their immediate family members; and

- **Analogous State and Foreign Laws**—Analogous state and foreign fraud and abuse laws and regulations, such as state anti-kickback and false claims laws, can apply to our business practices, including but not limited to research, distribution, sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third party payors and are generally broad and are enforced by many different federal and state agencies as well as through private actions.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and require manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures and pricing information. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not pre-empted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties, and our business generally, 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, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. Defending against any such actions can be costly, time-consuming and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired. If any of the physicians or other healthcare providers or entities with whom we expect to do business is 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.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is generally not permitted in the countries that form part of the European Union. Some European Union Member States, like the United Kingdom, through the United Kingdom Bribery Act 2010, have enacted laws explicitly prohibiting the provision of these type of benefits and advantages. Infringements of these laws can result in substantial fines and imprisonment.

Payments made to physicians in certain European Union Member States (e.g., France or Belgium) must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual European Union Member States. These requirements are provided in the European Union Member State national laws, industry codes (e.g. the European Federation of Pharmaceutical Industries and Associations Disclosure and Healthcare Professionals Codes) or professional codes of conduct. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

The collection and processing of personal data – including health data – in the European Union is currently governed by the provisions of the Data Protection Directive, as implemented into national laws by the European Union Member States. The new European Union-wide General Data Protection Regulation, or GDPR, entered into force in May 2016 and will become applicable on May 25, 2018, replacing the current data protection laws of each European Union Member State. The GDPR will implement more stringent operational requirements 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, increased requirements pertaining to health data and pseudonymised (i.e., key-coded) data, mandatory data breach notification requirements and higher standards for controllers to demonstrate that they have obtained valid consent for certain data processing activities. The GDPR provides that European Union Member States may make their own further laws and regulations in relation to the processing of genetic, biometric or health data, which could result in differences between Member States, limit our ability to use and share personal data or could cause our costs to increase, and harm our business and financial condition. We are also subject to evolving and strict rules on the transfer of personal data out of the European Union to the United States. Failure to comply with European Union data protection laws may result in fines (for example, of up to €20,000,000 or up to 4% of the total worldwide annual turnover of the preceding financial year (whichever is higher) under the GDPR) and other administrative penalties, which may be onerous and adversely affect our business, financial condition, results of operations and prospects.

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

In the United States and foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay regulatory approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain regulatory approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and in additional downward pressure on the price that we, or any collaborators, may receive for any approved products.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the ACA. Among the provisions of the ACA of potential importance to our business and our product candidates are the following:

- an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription products and biologic products;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for products that are inhaled, infused, instilled, implanted or injected;
- expansion of healthcare fraud and abuse laws, including the civil False Claims Act and the federal 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 of applicable brand products to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient products to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to individuals enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report certain financial arrangements with physicians and teaching hospitals;
- a new requirement to annually report product samples that manufacturers and distributors provide to physicians;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- a new Independent Payment Advisory Board, or IPAB, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription products; and
- established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, included aggregate reductions to Medicare payments to providers of 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2025 unless additional Congressional action is taken. The American Taxpayer Relief Act of 2012, 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 new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

With the new Administration and Congress, there will likely be additional administrative or legislative changes, including modification, repeal, or replacement of all, or certain provisions of, the ACA. In January 2017, Congress voted to adopt a budget resolution for fiscal year 2017, or the Budget Resolution, that authorizes the implementation of legislation that would repeal portions of the ACA. The Budget Resolution is not a law, however, it is widely viewed as the first step toward

the passage of legislation that would repeal certain aspects of the ACA. Further, 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 or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices.

At the same time, Congress has focused on additional legislative changes, including in particular repeal and replacement of certain provisions of the ACA. It remains to be seen, however, whether new legislation reforming, repealing or replacing the ACA will be enacted and, if so, precisely what the new legislation will provide and what impact it will have on the availability of healthcare and containing or lowering the cost of healthcare. It is possible that these reform, repeal and replacement initiatives, if enacted into law, could ultimately result in fewer individuals having health insurance coverage or in individuals having insurance coverage with less generous benefits. It is also possible that some ACA provisions that generally are not favorable for the research-based pharmaceutical industry could also be repealed along with ACA coverage expansion provisions. At this point, healthcare reform and its impacts on us are highly uncertain in many respects.

The costs of prescription pharmaceuticals in the United States has also been the subject of considerable discussion in the United States, and members of Congress and the Administration have stated that they will address such costs through new legislative and administrative measures. There have been several U.S. Congressional inquiries and proposed bills designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs.

In addition, individual states have also become increasingly active in passing legislation and implementing regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access, and to encourage importation from other countries and bulk purchasing.

The pricing of prescription pharmaceuticals is also subject to governmental control outside the United States. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of regulatory approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidates to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our ability to generate revenues and become profitable could be impaired.

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

In some countries, including Member States of the European Union, the pricing of prescription drugs is subject to governmental control. Additional countries may adopt similar approaches to the pricing of prescription drugs. In such countries, pricing negotiations with governmental authorities can take considerable time after receipt of regulatory approval for a product. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after coverage and reimbursement have been obtained. Reference pricing used by various countries and parallel distribution, or arbitrage between low-priced and high-priced countries, can further reduce prices. In some countries, we may be required to conduct a clinical study or other studies that compare the cost-effectiveness of any of our product candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval, which is time-consuming and costly. We cannot be sure that such prices and reimbursement will be acceptable to us or our strategic partners. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If pricing is set at unsatisfactory levels or if reimbursement of our products is unavailable or limited in scope or amount, our revenues from sales by us or our strategic partners and the potential profitability of any of our product candidates in those countries would be negatively affected.

Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing and selling certain products outside of the United States and require us to develop and implement costly compliance programs.

If we further expand our operations outside of the United States, we must dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate. The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of

the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring us to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the United States, it will require us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain products and product candidates outside of the United States, which could limit our growth potential and increase our development costs.

The failure to comply with laws governing international business practices may result in substantial civil and criminal penalties and suspension or debarment from government contracting. The Securities and Exchange Commission, or SEC, also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. From time to time and in the future, our operations may involve the use of hazardous and flammable materials, including chemicals and biological materials, and may also produce hazardous waste products. Even if we contract with third parties for the disposal of these materials and waste products, we cannot completely eliminate the risk of contamination or injury resulting from these materials. In the event of contamination or injury resulting from the use or disposal of our hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

We maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees, but this insurance may not provide adequate coverage against potential liabilities. However, we do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. Current or future environmental laws and regulations may impair our research, development or production efforts. In addition, failure to comply with these laws and regulations may result in substantial fines, penalties or other sanctions.

Risks Related to Our Intellectual Property

Our commercial success depends on our ability to protect our intellectual property and proprietary technology.

Our commercial success depends in large part on our ability to obtain and maintain intellectual property rights protection through patents, trademarks, and trade secrets in the United States and other countries with respect to our proprietary product candidates. If we do not adequately protect our intellectual property rights, competitors may be able to erode, negate or preempt any competitive advantage we may have, which could harm our business and ability to achieve profitability. To protect our proprietary position, we have patent applications and may file other patent applications in the United States or abroad related to our product candidates that are important to our business; we may also license or purchase patent applications filed by others. The patent application and approval process is expensive and time-consuming. We may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner.

Agreements through which we license patent rights may not give us control over patent prosecution or maintenance, so that we may not be able to control which claims or arguments are presented, how claims are amended, and may not be able to secure, maintain, or successfully enforce necessary or desirable patent protection from those patent rights. We have not had and do not have primary control over patent prosecution and maintenance for certain of the patents and patent applications we license, and therefore cannot guarantee that these patents and applications will be prosecuted or maintained in a manner consistent with the best interests of our business. We cannot be certain that patent prosecution and maintenance activities by our licensors have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents.

If the scope of the patent protection we or our licensors obtain is not sufficiently broad, we may not be able to prevent others from developing and commercializing technology and products similar or identical to ours. The degree of patent protection we require to successfully compete in the marketplace may be unavailable or severely limited in some cases and may not adequately protect our rights or permit us to gain or keep any competitive advantage. We cannot provide any assurances that any of our licensed patents have, or that any of our pending owned or licensed patent applications that mature into issued patents will include, claims with a scope sufficient to protect our proprietary platform or otherwise provide any competitive advantage, nor can we assure you that our licenses are or will remain in force. Other parties have developed or may develop technologies that may be related or competitive with our approach, and may have filed or may file patent applications and may have been issued or may be issued patents with claims that overlap or conflict with our patent applications, either by claiming the same compounds, formulations or methods or by claiming subject matter that could dominate our patent position. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Furthermore, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally twenty years after it is filed. Various extensions may be available; however, the life of a patent, and the protection it affords, is limited. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with adequate and continuing patent protection sufficient to exclude others from commercializing products similar to our product candidates. In addition, the patent portfolio licensed to us is, or may be, licensed to third parties, such as outside our field, and such third parties may have certain enforcement rights. Thus, patents licensed to us could be put at risk of being invalidated or interpreted narrowly in litigation filed by or against another licensee or in administrative proceedings brought by or against another licensee in response to such litigation or for other reasons.

Even if they are unchallenged, our owned and licensed patents and pending patent applications, if issued, may not provide us with any meaningful protection or prevent competitors from designing around our patent claims to circumvent our patents by developing similar or alternative technologies or therapeutics in a non-infringing manner. For example, a third party may develop a competitive therapy that provides benefits similar to one or more of our product candidates but falls outside the scope of our patent protection or license rights. If the patent protection provided by the patents and patent applications we hold or pursue with respect to our product candidates is not sufficiently broad to impede such competition, our ability to successfully commercialize our product candidates could be negatively affected, which would harm our business. Currently, a significant portion of our patents and patent applications are in-licensed, though similar risks would apply to any patents or patent applications that we now own or may own or in-license in the future.

We, or any future partners, collaborators, or licensees, may fail to identify patentable aspects of inventions made in the course of development and commercialization activities before it is too late to obtain patent protection on them. Therefore, we may miss potential opportunities to strengthen our patent position.

It is possible that defects of form in the preparation or filing of our patents or patent applications may exist, or may arise in the future, for example with respect to proper priority claims, inventorship, claim scope, or requests for patent term adjustments. If we or our partners, collaborators, licensees, or licensors, whether current or future, fail to establish, maintain or protect such patents and other intellectual property rights, such rights may be reduced or eliminated. If our partners, collaborators, licensees, or licensors, are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised. If there are material defects in the form, preparation, prosecution, or enforcement of our patents or patent applications, such patents may be invalid and/or unenforceable, and such applications may never result in valid, enforceable patents. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

The patent position of biotechnology and pharmaceutical companies carries uncertainty. In addition, the determination of patent rights with respect to pharmaceutical compounds commonly involves complex legal and factual questions, which are dependent upon the current legal and intellectual property context, extant legal precedent and interpretations of the law by individuals. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are characterized by uncertainty.

Pending patent applications cannot be enforced against third parties practicing the technology claimed in such applications unless and until a patent issues from such applications. Assuming the other requirements for patentability are met, currently, the first to file a patent application is generally entitled to the patent. However, prior to March 16, 2013, in the United States, the first to invent was entitled to the patent. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. Similarly, we cannot be certain that parties from whom we do or may license or purchase patent rights were the first to make relevant claimed inventions, or were the first to file for patent protection for them. If third parties have filed prior patent applications on inventions claimed in our patents or applications that were filed on or before March 15, 2013, an interference proceeding in the United States can be initiated by such third parties to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. If third parties have filed such prior applications after March 15, 2013, a derivation proceeding in the United States can be initiated by such third parties to determine whether our invention was derived from theirs.

Moreover, because the issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, our patents or pending patent applications may be challenged in the courts or patent offices in the United States and abroad. There is no assurance that all of the potentially relevant prior art relating to our patents and patent applications has been found. If such prior art exists, it may be used to invalidate a patent, or may prevent a patent from issuing from a pending patent application. For example, such patent filings may be subject to a third-party submission of prior art to the U.S. Patent and Trademark Office, or USPTO, or to other patent offices around the world. Alternately or additionally, we may become involved in post-grant review procedures, oppositions, derivation proceedings, *ex parte* reexaminations, *inter partes* review, supplemental examinations, or interference proceedings or challenges in district court, in the United States or in various foreign patent offices, including both national and regional, challenging patents or patent applications in which we have rights, including patents on which we rely to protect our business. An adverse determination in any such challenges may result in loss of the patent or in patent or patent application claims being narrowed, invalidated or held unenforceable, in whole or in part, or in denial of the patent application or loss or reduction in the scope of one or more claims of the patent or patent application, any of which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. In addition, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized.

Pending and future patent applications may not result in patents being issued that protect our business, in whole or in part, or which effectively prevent others from commercializing competitive products. Competitors may also be able to design around our patents. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. In addition, the laws of foreign countries may not protect our rights to the same extent or in the same manner as the laws of the United States. For example, patent laws in various jurisdictions, including significant commercial markets such as Europe, restrict the patentability of methods of treatment of the human body more than United States law does. If these developments were to occur, they could have a material adverse effect on our ability to generate revenue.

The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our future development partners will be successful in protecting our product candidates by obtaining and defending patents. These risks and uncertainties include the following:

- the USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case;

- patent applications may not result in any patents being issued;

- patents that may be issued or in-licensed may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable or otherwise may not provide any competitive advantage;

- our competitors, many of whom have substantially greater resources and many of whom have made significant investments in competing technologies, may seek or may have already obtained patents that will limit, interfere with or eliminate our ability to make, use, and sell our potential product candidates;

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

- countries other than the United States may have patent laws less favorable to patentees than those upheld by U.S. courts, allowing foreign competitors a better opportunity to create, develop and market competing product candidates.

Issued patents that we have or may obtain or license may not provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our patents by developing similar or alternative technologies or products in a non-infringing manner. Our competitors may also seek approval to market their own products similar to or otherwise competitive with our products. Alternatively, our competitors may seek to market generic versions of any approved products by submitting ANDAs to the FDA in which they claim that patents owned or licensed by us are invalid, unenforceable or not infringed. In these circumstances, we may need to defend or assert our patents, or both, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or other agency with jurisdiction may find our patents invalid or unenforceable, or that our competitors are competing in a non-infringing manner. Thus, even if we have valid and enforceable patents, these patents still may not provide protection against competing products or processes sufficient to achieve our business objectives.

In addition, we rely on the protection of our trade secrets and proprietary, unpatented know-how. Although we have taken steps to protect our trade secrets and unpatented know-how, including entering into confidentiality agreements with third parties, and confidential information and invention assignment agreements with employees, consultants, collaborators, vendors, and advisors, we cannot provide any assurances that all such agreements have been duly executed, and third parties may still obtain this information or may come upon this or similar information independently. It is possible that technology relevant to our business will be independently developed by a person who is not a party to such a confidentiality or invention assignment agreement. We may not be able to prevent the unauthorized disclosure or use of our technical knowledge or trade secrets by consultants, collaborators, vendors, advisors, former employees and current employees. Furthermore, if the parties to our confidentiality agreements breach or violate the terms of these agreement, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets as a consequence of such breaches or violations. Our trade secrets could otherwise become known or be independently discovered by our competitors. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating our trade secrets. If any of these events occurs or if we otherwise lose protection for our trade secrets or proprietary know-how, our business may be harmed.

We depend on intellectual property licensed from third parties and termination of any of these licenses could result in the loss of significant rights, which would harm our business.

In March 2017, we entered into a license agreement with Novartis, or the Novartis License, pursuant to which we were granted an exclusive, field-restricted, worldwide license to certain intellectual property rights owned or controlled by Novartis, including patents, patent applications, proprietary information, know-how and other intellectual property, to develop, commercialize and sell one or more therapeutic products comprising RTB101 or RTB101 and everolimus in a fixed dose combination.

We are dependent on these patents, know-how and proprietary technology, licensed from Novartis. Any termination of this license, or a finding that such intellectual property lacks legal effect, could result in the loss of significant rights and could harm our ability to commercialize any product candidates. See the section entitled “Business—Intellectual Property” for additional information regarding our license agreements.

Disputes may also arise between us and our licensor, our licensor and its licensors, or us and third parties that co-own intellectual property with our licensor or its licensors, regarding intellectual property subject to a license agreement, including those relating to:

- the scope of rights, if any, granted under the license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the license agreement;
- whether our licensor or its licensor had the right to grant the license agreement;
- whether third parties are entitled to compensation or equitable relief, such as an injunction, for our use of the intellectual property without their authorization;
- our right to sublicense patent and other rights to third parties under collaborative development relationships;
- whether we are complying with our obligations with respect to the use of the licensed technology in relation to our development and commercialization of product candidates;
- our involvement in the prosecution of the licensed patents and our licensors' overall patent enforcement strategy;
- the allocation of ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and by us and our partners; and
- the amounts of royalties, milestones or other payments due under the license agreement.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, or are insufficient to provide us the necessary rights to use the intellectual property, we may be unable to successfully develop and commercialize the affected product candidates. If we or any such licensors fail to adequately protect this intellectual property, our ability to commercialize our products could suffer.

Novartis may partially terminate the license agreement with respect to everolimus if we fail or cease for three years to use commercially reasonable efforts to research, develop and commercialize a product using everolimus, provided that our license related to RTB101 and Novartis's license to our improvements related to everolimus will continue. Additionally, either party may terminate the Novartis License if the other party commits a material breach and fails to cure such breach within 60 days after written notice. If Novartis unilaterally terminates the Novartis License, the research and development of RTB101 or RTB101 and everolimus in a fixed dose combination would be suspended, and we may be unable to research, develop and license future product candidates.

We may be required to pay certain milestones and royalties under our license agreements with third-party licensors.

Under our current and future license agreements, we may be required to pay milestones and royalties based on our revenues from sales of our products utilizing the technologies licensed or sublicensed from Novartis or other licensors and these royalty payments could adversely affect the overall profitability for us of any products that we may seek to commercialize. In order to maintain our license rights under current and future license agreements, we may need to meet certain specified milestones, subject to certain cure provisions, in the development of our product candidates and in the raising of funding. In addition, these agreements may contain diligence milestones and we may not be successful in meeting all of the milestones in the future on a timely basis or at all, which could result in termination of our rights under such agreements. We may need to outsource and rely on third parties for many aspects of the clinical development, sales and marketing of our products covered under our current and future license agreements. Delay or failure by these third parties could adversely affect the continuation of our license agreements with their third-party licensors.

It is difficult and costly to protect our intellectual property and our proprietary technologies, and we may not be able to ensure their protection.

Our commercial success will depend in part on obtaining and maintaining patent protection and trade secret protection for the use, formulation and structure of our products and product candidates, the methods used to manufacture them, the related therapeutic targets and associated methods of treatment as well as on successfully defending these patents against potential third-party challenges. Our ability to protect our products and product candidates from unauthorized making, using, selling, offering to sell or importing by third parties is dependent on the extent to which we have rights under valid and enforceable patents that cover these activities.

The patent positions of pharmaceutical, biotechnology and other life sciences companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. Changes in either the patent laws or in interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property. Further, the determination that a patent application or patent claim meets all of the requirements for patentability is a subjective determination based on the application of law and jurisprudence. The ultimate determination by the USPTO or by a court or other trier of fact in the United States, or corresponding foreign national patent offices or courts, on whether a claim meets all requirements of patentability cannot be assured. Although we have conducted searches for third-party publications, patents and other information that may affect the patentability of claims in our various patent applications and patents, we cannot be certain that all relevant information has been identified. Accordingly, we cannot predict the breadth of claims that may be allowed or enforced in our owned patents or patent applications, in our licensed patents or patent applications or in third-party patents.

We cannot provide assurances that any of our patent applications will be found to be patentable, including over our own or our licensors' prior art publications or patent literature, or will issue as patents. Neither can we make assurances as to the scope of any claims that may issue from our pending and future patent applications nor to the outcome of any proceedings by any potential third parties that could challenge the patentability, validity or enforceability of our patents and patent applications in the United States or foreign jurisdictions. Any such challenge, if successful, could limit patent protection for our products and product candidates and/or materially harm our business.

The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- we may not be able to generate sufficient data to support full patent applications that protect the entire breadth of developments in one or more of our programs;
- it is possible that one or more of our pending patent applications will not become an issued patent or, if issued, that the patent(s) claims will have sufficient scope to protect our technology, provide us with a basis for commercially viable products or provide us with any competitive advantages;
- if our pending applications issue as patents, they may be challenged by third parties as not infringed, invalid or unenforceable under United States or foreign laws;
- if issued, the patents under which we hold rights may not be valid or enforceable;
- we may not successfully commercialize RTB101, alone or in combination with everolimus, if approved, before our relevant patents expire;
- we may not be the first to make the inventions covered by each of our patents and pending patent applications; or
- we may not develop additional proprietary technologies or product candidates that are separately patentable.

In addition, to the extent that we are unable to obtain and maintain patent protection for one of our products or product candidates or in the event that such patent protection expires, it may no longer be cost-effective to extend our portfolio by pursuing additional development of a product or product candidate for follow-on indications.

We also may rely on trade secrets to protect our technologies or products, especially where we do not believe patent protection is appropriate or obtainable. Also, we cannot provide any assurances that any of our licensed patents have claims with a scope sufficient to protect our technology or otherwise provide any competitive advantage, nor can we assure you that our licenses are or will remain in full force or effect, in which case we would similarly rely on trade secrets. However, trade secrets are difficult to protect. Although we use reasonable efforts to protect our trade secrets, our employees, consultants, contractors, outside scientific collaborators and other advisers may unintentionally or willfully disclose our information to competitors. Enforcing a claim that a third-party entity illegally obtained and is using any of our trade secrets is expensive and time-consuming, and the outcome is unpredictable. In addition, courts outside the United States are sometimes less willing to protect trade secrets. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how. Notably, proprietary technology protected by a trade secret does not preempt the patenting of independently developed equivalent technology, even if such equivalent technology is invented subsequent to the technology protected by a trade secret.

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

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and applications are required to be paid to the USPTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and applications. The USPTO and various non-U.S. governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process and after a patent has issued. There are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such a circumstance, competitors may be able to enter the market earlier than otherwise would be the case. Under the terms of some of our current and future licenses, we may not have the ability to maintain patents or prosecute patent applications in the portfolio, and may therefore have to rely on third parties to comply with these requirements.

Patent terms may be inadequate to protect our competitive position on our products for an adequate amount of time.

Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. We expect to seek extensions of patent terms in the United States and, if available, in other countries where we are prosecuting patents. In the United States, the Drug Price Competition and Patent Term Restoration Act of 1984 permits a patent term extension of up to five years beyond the normal expiration of the patent, which is limited to the approved indication (or any additional indications approved during the period of extension). We might not be granted an extension because of, for example, failure to apply within applicable periods, failure to apply prior to the expiration of relevant patents or otherwise failure to satisfy any of the numerous applicable requirements. Moreover, the applicable authorities, including the FDA and the USPTO in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. If this occurs, our competitors may be able to obtain approval of competing products following our patent expiration by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case. If this were to occur, it could have a material adverse effect on our ability to generate revenue.

Changes to patent law in the United States and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with other biopharmaceutical companies, our commercial success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involves both technological and legal complexity and is therefore costly, time consuming and inherently uncertain. Recent wide-ranging patent reform legislation in the United States, including the Leahy-Smith America Invents Act, or the America Invents Act, could increase those uncertainties and costs. The America Invents Act was signed into law on September 16, 2011, and many of the substantive changes became effective on March 16, 2013. The America Invents Act reforms United States patent law in part by changing the U.S. patent system from a “first to invent” system to a “first inventor to file” system, expanding the definition of prior art, and developing a post-grant review system. This legislation changes United States patent law in a way that may weaken our ability to obtain patent protection in the United States for those applications filed after March 16, 2013.

Further, the America Invents Act created new procedures to challenge the validity of issued patents in the United States, including post-grant review and *inter partes* review proceedings, which some third parties have been using to cause the cancellation of selected or all claims of issued patents of competitors. For a patent with an effective filing date of March 16, 2013 or later, a petition for post-grant review can be filed by a third party in a nine month window from issuance of the patent. A petition for *inter partes* review can be filed immediately following the issuance of a patent if the patent has an effective filing date prior to March 16, 2013. A petition for *inter partes* review can be filed after the nine month period for filing a post-grant review petition has expired for a patent with an effective filing date of March 16, 2013 or later. Post-grant review proceedings can be brought on any ground of invalidity, whereas *inter partes* review proceedings can only raise an invalidity challenge based on published prior art and patents. These adversarial actions at the USPTO review patent claims without the presumption of validity afforded to U.S. patents in lawsuits in U.S. federal courts, and use a lower burden of proof than used in litigation in U.S. federal courts. Therefore, it is generally considered easier for a competitor or third party to have a U.S. patent invalidated in a USPTO post-grant review or *inter partes* review proceeding than invalidated in a litigation in a U.S. federal court. If any of our patents are challenged by a third party in such a USPTO proceeding, there is no guarantee that we or our licensors or collaborators will be successful in defending the patent, which may result in a loss of the challenged patent right to us.

In addition, recent court rulings in cases such as *Association for Molecular Pathology v. Myriad Genetics, Inc., BRCA1- & BRCA2-Based Hereditary Cancer Test Patent Litigation, and Promega Corp. v. Life Technologies Corp.* have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents once obtained. Depending on future actions by the U.S. Congress, the U.S. courts, the USPTO and the relevant law-making bodies in other countries, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

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

Filing, prosecuting, enforcing and defending patents on our product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. The requirements for patentability may differ in certain countries, particularly in developing countries; thus, even in countries where we do pursue patent protection, there can be no assurance that any patents will issue with claims that cover our products.

Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws. Additionally, laws of some countries outside of the United States and Europe do not afford intellectual property protection to the same extent as the laws of the United States and Europe. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, including India, China and other developing countries, do not favor the enforcement of patents and other intellectual property rights. This could make it difficult for us to stop the infringement of our patents or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. Consequently, we may not be able to prevent third parties from practicing our inventions in certain countries outside the United States and Europe or from selling or importing products made from our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop and market their own products and, further, may export otherwise infringing products to territories where we have patent protection, if our ability to enforce our patents to stop infringing activities is inadequate. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Agreements through which we license patent rights may not give us sufficient rights to permit us to pursue enforcement of our licensed patents or defense of any claims asserting the invalidity of these patents (or control of such enforcement or defense) of such patent rights in all relevant jurisdictions as requirements may vary.

Proceedings to enforce our patent rights, whether or not successful, could result in substantial costs and divert our efforts and resources from other aspects of our business. Moreover, such proceedings could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Furthermore, while we intend to protect our intellectual property rights in major markets for our products, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our products, if approved. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate.

Others may challenge inventorship or claim an ownership interest in our intellectual property which could expose it to litigation and have a significant adverse effect on its prospects.

A third party or former employee or collaborator may claim an ownership interest in one or more of our or our licensors' patents or other proprietary or intellectual property rights. A third party could bring legal actions against us and seek monetary damages and/or enjoin clinical testing, manufacturing and marketing of the affected product or products. While we are presently unaware of any claims or assertions by third-parties with respect to our patents or other intellectual property, we cannot guarantee that a third party will not assert a claim or an interest in any of such patents or intellectual property. If we become involved in any litigation, it could consume a substantial portion of our resources, and cause a significant diversion of effort by our technical and management personnel.

If we are sued for infringing intellectual property rights of third parties, such litigation could be costly and time consuming and could prevent or delay us from developing or commercializing our product candidates.

Our commercial success depends, in part, on our ability to develop, manufacture, market and sell our product candidates without infringing the intellectual property and other proprietary rights of third parties. Third parties may have U.S. and non-U.S. issued patents and pending patent applications relating to compounds, methods of manufacturing compounds and/or methods of use for the treatment of the disease indications for which we are developing our product candidates. If any third-party patents or patent applications are found to cover our product candidates or their methods of use or manufacture, we may not be free to manufacture or market our product candidates as planned without obtaining a license, which may not be available on commercially reasonable terms, or at all.

There is a substantial amount of intellectual property litigation in the biotechnology and pharmaceutical industries, and we may become party to, or threatened with, litigation or other adversarial proceedings regarding intellectual property rights with respect to our products candidates, including interference and post-grant proceedings before the USPTO. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the composition, use or manufacture of our product candidates. We cannot guarantee that any of our patent searches or analyses including, but not limited to, the identification of relevant patents, the scope of patent claims or the expiration of relevant patents are complete or thorough, nor can we be certain that we have identified each and every patent and pending application in the United States and abroad that is relevant to or necessary for the commercialization of our product candidates in any jurisdiction. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may be accused of infringing. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Accordingly, third parties may assert infringement claims against us based on intellectual property rights that exist now or arise in the future. The outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance. The pharmaceutical and biotechnology industries have produced a significant number of patents, and it may not always be clear to industry participants, including us, which patents cover various types of products or methods of use or manufacture. The scope of protection afforded by a patent is subject to interpretation by the courts, and the interpretation is not always uniform. If we were sued for patent infringement, we would need to demonstrate that our product candidates, products or methods either do not infringe the patent claims of the relevant patent or that the patent claims are invalid or unenforceable, and we may not be able to do this. Proving invalidity is difficult. For example, in the United States, proving invalidity requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents. Even if we are successful in these proceedings, we may incur substantial costs and the time and attention of our management and scientific personnel could be diverted in pursuing these proceedings, which could significantly harm our business and operating results. In addition, we may not have sufficient resources to bring these actions to a successful conclusion.

If we are found to infringe a third party's intellectual property rights, we could be forced, including by court order, to cease developing, manufacturing or commercializing the infringing product candidate or product. Alternatively, we may be required to obtain a license from such third party in order to use the infringing technology and continue developing, manufacturing or marketing the infringing product candidate or product. If we were required to obtain a license to continue to manufacture or market the affected product, we may be required to pay substantial royalties or grant cross-licenses to our patents. We cannot, however, assure you that any such license will be available on acceptable terms, if at all. Ultimately, we could be prevented from commercializing a product, or be forced to cease some aspect of our business operations as a result of claims of patent infringement or violation of other intellectual property rights, Further, the outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance, including the demeanor and credibility of witnesses and the identity of any adverse party. This is especially true in intellectual property cases that may turn on the testimony of experts as to technical facts upon which experts may reasonably disagree. Furthermore, we may not be able to

obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us; alternatively or additionally it could include terms that impede or destroy our ability to compete successfully in the commercial marketplace. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations, which could harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

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

Many of our current and former employees and our licensors' current and former employees, including our senior management, were previously employed at universities or at other biotechnology or pharmaceutical companies, including some which may be competitors or potential competitors. Some of these employees, including members of our senior management, may have executed proprietary rights, non-disclosure and non-competition agreements, or similar agreements, in connection with such previous employment. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such third party. Litigation may be necessary to defend against such claims. If we fail in defending any such claims, in addition to paying monetary damages, we may sustain damages or lose key personnel, valuable intellectual property rights or the personnel's work product, which could hamper or prevent commercialization of our technology, which could materially affect our commercial development efforts. Such intellectual property rights could be awarded to a third party, and we could be required to obtain a license from such third party to commercialize our technology or products. Such a license may not be available on commercially reasonable terms or at all. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

In addition, while we typically require our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own, which may result in claims by or against us related to the ownership of such intellectual property. If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our senior management and scientific personnel.

We may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our patents, trademarks, copyrights or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time consuming and divert the time and attention of our management and scientific personnel. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents, in addition to counterclaims asserting that our patents are invalid or unenforceable, or both. In any patent infringement proceeding, there is a risk that a court will decide that a patent of ours is invalid or unenforceable, in whole or in part, and that we do not have the right to stop the other party from using the invention at issue. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent's claims narrowly or decide that we do not have the right to stop the other party from using the invention at issue on the grounds that our patent claims do not cover the invention. An adverse outcome in a litigation or proceeding involving one or more of our patents could limit our ability to assert those patents against those parties or other competitors, and may curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the trademarks in question. In this case, we could ultimately be forced to cease use of such trademarks.

Even if we establish infringement, the court may decide not to grant an injunction against further infringing activity and instead award only monetary damages, which may or may not be an adequate remedy. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive

these results to be negative, it could adversely affect the price of shares of our common stock. Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive as a result of the proceedings.

Additionally, for certain of our existing and future in-licensed patent rights, we may not have the right to bring suit for infringement and may have to rely on third parties to enforce these rights for us. If we cannot or choose not to take action against those we believe infringe our intellectual property rights, we may have difficulty competing in certain markets where such potential infringers conduct their business, and our commercialization efforts may suffer as a result.

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

Our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We rely on both registration and common law protection for our trademarks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. During trademark registration proceedings, we may receive rejections. Although we would be given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. Moreover, any name we propose to use for our products in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA objects to any of our proposed product names, we may be required to expend significant additional resources in an effort to identify a usable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected.

Risks Related to Our Dependence on Third Parties

We rely on third parties to assist in conducting our clinical trials. If they do not perform satisfactorily, we may not be able to obtain regulatory approval or commercialize our product candidates, or such approval or commercialization may be delayed, and our business could be substantially harmed.

We do not independently conduct clinical trials of any of our product candidates. We have relied upon and plan to continue to rely on third parties, such as contract research organizations, clinical data management organizations, medical institutions and clinical investigators, to conduct these clinical trials and expect to rely on these third parties to conduct clinical trials of any other product candidate that we develop. Any of these third parties may terminate their engagements with us under certain circumstances. We may not be able to enter into alternative arrangements or do so on commercially reasonable terms. In addition, there is a natural transition period when a new CRO begins work. As a result, delays may occur, which could negatively impact our ability to meet our expected clinical development timelines and harm our business, financial condition and prospects.

Further, although our reliance on these third parties for clinical development activities limits our control over these activities, we remain responsible for ensuring that each of our trials is conducted in accordance with the applicable protocol, legal and regulatory requirements and scientific standards. For example, notwithstanding the obligations of a CRO for a trial of one of our product candidates, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with requirements, commonly referred to as Good Clinical Practices, or GCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. The FDA enforces these GCPs through periodic inspections of trial sponsors, principal investigators, clinical trial sites and IRBs. If we or our third-party contractors fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving our product candidates, which would delay the regulatory approval process. We cannot be certain that, upon inspection, the FDA will determine that any of our clinical trials comply with GCPs. We are also required to register certain clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Furthermore, the third parties conducting clinical trials on our behalf are not our employees, and except for remedies available to us under our agreements with such contractors, we cannot control whether or not they devote sufficient time, skill and resources to our ongoing development programs. These contractors may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities, which could impede their ability to devote appropriate time to our clinical programs. If these third parties, including clinical investigators, do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we may not be able to obtain, or may be delayed in obtaining, regulatory approvals for our product candidates. If that occurs, we will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates. In such an event, our financial results and the commercial prospects for any product candidates that we seek to develop could be harmed, our costs could increase and our ability to generate revenues could be delayed, impaired or foreclosed.

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

Our use of third parties to manufacture our product candidates and products which we are studying in combination with our product candidates may increase the risk that we will not have sufficient quantities of our product candidates, products, or necessary quantities of such materials on time or at an acceptable cost.

We do not own or operate manufacturing facilities for the production of clinical or commercial quantities of our product candidates, and we lack the resources and the capabilities to do so. As a result, we currently rely on third parties for the manufacture and supply of the active pharmaceutical ingredients, or API, in our product candidates. Our current strategy is to outsource all manufacturing of our product candidates to third parties.

We currently engage one third-party manufacturer to provide the active pharmaceutical ingredient, or API, and four other third-party manufacturers to provide services for the final drug product formulation of RTB101 that is being used in our clinical trials. Although we believe that there are several potential alternative manufacturers who could manufacture RTB101 and everolimus, we may incur added costs and delays in identifying and qualifying any such replacement. In addition, we typically order raw materials and services on a purchase order basis and do not enter into long-term dedicated capacity or minimum supply arrangements with any commercial manufacturer. There is no assurance that we will be able to timely secure needed supply arrangements on satisfactory terms, or at all. Our failure to secure these arrangements as needed could have a material adverse effect on our ability to complete the development of our product candidates or, to commercialize them, if approved. We may be unable to conclude agreements for commercial supply with third-party manufacturers, or may be unable to do so on acceptable terms. There may be difficulties in scaling up to commercial quantities and formulation of RTB101, alone or in combination with everolimus, and the costs of manufacturing could be prohibitive.

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

- the failure of the third-party manufacturer to comply with applicable regulatory requirements and reliance on third-parties for manufacturing process development, regulatory compliance and quality assurance;
- manufacturing delays if our third-party manufacturers give greater priority to the supply of other products over our product candidates or otherwise do not satisfactorily perform according to the terms of the agreement between us;
- limitations on supply availability resulting from capacity and scheduling constraints of third-parties;
- the possible breach of manufacturing agreements by third-parties because of factors beyond our control;
- the possible termination or non-renewal of the manufacturing agreements by the third-party, at a time that is costly or inconvenient to us; and
- the possible misappropriation of our proprietary information, including our trade secrets and know-how.

If we do not maintain our key manufacturing relationships, we may fail to find replacement manufacturers or develop our own manufacturing capabilities, which could delay or impair our ability to obtain regulatory approval for our products. If we do find replacement manufacturers, we may not be able to enter into agreements with them on terms and conditions favorable to us and there could be a substantial delay before new facilities could be qualified and registered with the FDA and other foreign regulatory authorities.

If any of our product candidates are approved by any regulatory agency, we intend to utilize arrangements with third-party contract manufacturers for the commercial production of those products. This process is difficult and time consuming and we may face competition for access to manufacturing facilities as there are a limited number of contract manufacturers operating under cGMPs that are capable of manufacturing our product candidates. Consequently, we may not be able to reach agreement with third-party manufacturers on satisfactory terms, which could delay our commercialization.

Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, seizures or voluntary recalls of product candidates, operating restrictions and criminal prosecutions, any of which could significantly affect supplies of our product candidates. The facilities used by our contract manufacturers to manufacture our product candidates must be evaluated by the FDA pursuant to inspections that will be conducted after we submit our NDA to the FDA. We do not control the manufacturing process of, and are completely dependent on, our contract manufacturing partners for compliance with cGMPs. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, we may not be able to secure and/or maintain regulatory approval for our product manufactured at these facilities. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA finds deficiencies or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved. Contract manufacturers may face manufacturing or quality control problems causing drug substance production and shipment delays or a situation where the contractor may not be able to maintain compliance with the applicable cGMP requirements. Any failure to comply with cGMP requirements or other FDA, EMA and comparable foreign regulatory requirements could adversely affect our clinical research activities and our ability to develop our product candidates and market our products, if approved.

The FDA and other foreign regulatory authorities require manufacturers to register manufacturing facilities. The FDA and corresponding foreign regulators also inspect these facilities to confirm compliance with cGMPs. Contract manufacturers may face manufacturing or quality control problems causing drug substance production and shipment delays or a situation where the contractor may not be able to maintain compliance with the applicable cGMP requirements. Any failure to comply with cGMP requirements or other FDA, EMA and comparable foreign regulatory requirements could adversely affect our clinical research activities and our ability to develop our product candidates and market our products following approval.

If any third-party manufacturer of our product candidates is unable to increase the scale of its production of our product candidates, and/or increase the product yield of its manufacturing, then our costs to manufacture the product may increase and commercialization may be delayed.

In order to produce sufficient quantities to meet the demand for clinical trials and, if approved, subsequent commercialization of RTB101, alone or in combination with everolimus, or any other product candidates that we may develop, our third party manufacturer will be required to increase its production and optimize its manufacturing processes while maintaining the quality of the product. The transition to larger scale production could prove difficult. In addition, if our third party manufacturer is not able to optimize its manufacturing process to increase the product yield for our product candidates, or if it is unable to produce increased amounts of our product candidates while maintaining the quality of the product, then we may not be able to meet the demands of clinical trials or market demands, which could decrease our ability to generate profits and have a material adverse impact on our business and results of operation.

We may need to maintain licenses for active ingredients from third parties to develop and commercialize some of our product candidates, which could increase our development costs and delay our ability to commercialize those product candidates.

Should we decide to use active pharmaceutical ingredients in any of our product candidates that are proprietary to one or more third parties, we would need to maintain licenses to those active ingredients from those third parties. If we are unable to gain or continue to access rights to these active ingredients prior to conducting preclinical toxicology studies intended to support clinical trials, we may need to develop alternate product candidates from these programs by either accessing or developing alternate active ingredients, resulting in increased development costs and delays in commercialization of these product candidates. If we are unable to gain or maintain continued access rights to the desired active ingredients on commercially reasonable terms or develop suitable alternate active ingredients, we may not be able to commercialize product candidates from these programs.

Use of third parties to conduct testing of our product candidates in tissues or animals may increase the risk that we will have unsuitable or invalidated data for regulatory submissions and approval.

We currently do not own or operate laboratory facilities in which to conduct preclinical testing of our product candidates in tissues or animals. Preclinical studies regulated by FDA, EMA and most other health authorities are governed by Good Laboratory Practices, or GLP. Additionally, studies involving animals may be subject to further regulation by institutional, private or government animal welfare authorities that may vary by territory. Studies involving human tissues may also be subject to institutional and government human subject privacy policies that may vary by territory. Third party vendors conducting tissue and/or animal studies on our behalf may be found to be in violation of one or more of these regulations or policies and may be subject to closure, censure or other penalties. In some cases, these penalties could materially impact the performance, availability, or validity of studies conducted on our behalf. Even in the absence of violations resulting in penalties, regulatory and other authorities may refuse to authorize the conduct or to accept the results of studies for regulatory or ethical reasons.

We enter into various contracts in the normal course of our business in which we indemnify the other party to the contract. In the event we have to perform under these indemnification provisions, it could have a material adverse effect on our business, financial condition and results of operations.

In the normal course of business, we periodically enter into academic, commercial, service, collaboration, licensing, consulting and other agreements that contain indemnification provisions. With respect to our academic and other research agreements, we typically indemnify the institution and related parties from losses arising from claims relating to the products, processes or services made, used, sold or performed pursuant to the agreements for which we have secured licenses, and from claims arising from our exercise of rights under the agreement. With respect to our commercial agreements, we indemnify our vendors from any third-party product liability claims that could result from the production, use or consumption of the product, as well as for alleged infringements of any patent or other intellectual property right by a third party.

Should our obligation under an indemnification provision exceed applicable insurance coverage or if we were denied insurance coverage, our business, financial condition and results of operations could be adversely affected. Similarly, if we are relying on a collaborator to indemnify us and the collaborator is denied insurance coverage or the indemnification obligation exceeds the applicable insurance coverage and does not have other assets available to indemnify us, our business, financial condition and results of operations could be adversely affected.

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

We may seek one or more collaborators for the development and commercialization of one or more of our product candidates. Likely collaborators may include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. In addition, if we are able to obtain regulatory approval for product candidates from foreign regulatory authorities, we may enter into collaborations with international biotechnology or pharmaceutical companies for the commercialization of such product candidates.

We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator’s resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator’s evaluation of a number of factors. Those factors may include the potential differentiation of our product candidate from competing product candidates, design or results of

clinical trials, the likelihood of approval by the FDA, the EMA or comparable foreign regulatory authorities and the regulatory pathway for any such approval, the potential market for the product candidate, the costs and complexities of manufacturing and delivering the product to patients and the potential of competing products. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available for collaboration and whether such a collaboration could be more attractive than the one with us for our product candidate. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we may not be able to further develop our product candidates or bring them to market and generate product revenue.

Collaborations are complex and time-consuming to negotiate and document. Further, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. Any collaboration agreements that we enter into in the future may contain restrictions on our ability to enter into potential collaborations or to otherwise develop specified product candidates. We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of the product candidate for which we are seeking to collaborate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense.

If we enter into collaborations with third parties for the development and commercialization of our product candidates, our prospects with respect to those product candidates will depend in significant part on the success of those collaborations.

We may enter into collaborations for the development and commercialization of certain of our product candidates. If we enter into such collaborations, we will have limited control over the amount and timing of resources that our collaborators will dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on any future collaborators' abilities to successfully perform the functions assigned to them in these arrangements. In addition, any future collaborators may have the right to abandon research or development projects and terminate applicable agreements, including funding obligations, prior to or upon the expiration of the agreed upon terms.

Collaborations involving our product candidates pose a number of risks, including the following:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs, based on clinical trial results, changes in the collaborators' strategic focus or available funding or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our product candidates;
- a collaborator with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;
- disagreements with collaborators, including disagreements over proprietary rights, including trade secrets and intellectual property rights, contract interpretation, or the preferred course of development might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;

- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;

- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability; and

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

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If any future collaborator of ours is involved in a business combination, it could decide to delay, diminish or terminate the development or commercialization of any product candidate licensed to it by us.

We may have to alter our development and commercialization plans if we are not able to establish collaborations.

We will require additional funds to complete the development and potential commercialization of RTB101 alone or in combination with everolimus and other product candidates. For some of our product candidates, we may decide to collaborate with pharmaceutical and biotechnology companies for the development and potential commercialization of those product candidates.

We face significant competition in seeking and obtaining appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include:

- the design or results of clinical trials;

- the likelihood of approval by the FDA or comparable foreign regulatory authorities;

- the potential market for the subject product candidate;

- the costs and complexities of manufacturing and delivering such product candidate to patients;

- the potential for competing products;

- our patent position protecting the product candidate, including any uncertainty with respect to our ownership of our technology or our licensor's ownership of technology we license from them, which can exist if there is a challenge to such ownership without regard to the merits of the challenge;

- the need to seek licenses or sub-licenses to third-party intellectual property; and

- industry and market conditions generally.

The collaborator may also consider alternative product candidates or technologies for similar indications that may be available for collaboration and whether such a collaboration could be more attractive than the one with us for our product candidate. We may also be restricted under future license agreements from entering into agreements on certain terms with potential collaborators. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms, or at all, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund and undertake development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop our product candidates or bring them to market and our business may be materially and adversely affected.

Risks Related to Employee Matters and Managing Growth

We only have a limited number of employees to manage and operate our business.

As of March 23, 2018, we had seven full- or part-time employees. Our focus on the development of RTB101, alone or in combination with everolimus, requires us to optimize cash utilization and to manage and operate our business in a highly efficient manner. We cannot assure you that we will be able to hire and/or retain adequate staffing levels to develop RTB101, alone or in combination with everolimus, meet our obligations as a public company, run our operations and/or accomplish all of the objectives that we otherwise would seek to accomplish.

Cyber-attacks or other failures in our telecommunications or information technology systems, or those of our collaborators, contract research organizations, third-party logistics providers, distributors or other contractors or consultants, could result in information theft, data corruption and significant disruption of our business operations.

We, our collaborators, our CROs, third-party logistics providers, distributors and other contractors and consultants utilize information technology, or IT, systems and networks to process, transmit and store electronic information in connection with our business activities. As use of digital technologies has increased, cyber incidents, including deliberate attacks and attempts to gain unauthorized access to computer systems and networks, have increased in frequency and sophistication. These threats pose a risk to the security of our, our collaborators', our CROs', third-party logistics providers', distributors' and other contractors' and consultants' systems and networks, and the confidentiality, availability and integrity of our data. There can be no assurance that we will be successful in preventing cyber-attacks or successfully mitigating their effects. Similarly, there can be no assurance that our collaborators, CROs, third-party logistics providers, distributors and other contractors and consultants will be successful in protecting our clinical and other data that is stored on their systems. Any cyber-attack or destruction or loss of data could have a material adverse effect on our business and prospects. For example, the loss of clinical trial data from completed or ongoing clinical trials for any of our product candidates could result in delays in our development and regulatory approval efforts and significantly increase our costs to recover or reproduce the data. In addition, we may suffer reputational harm or face litigation or adverse regulatory action as a result of cyber-attacks or other data security breaches and may incur significant additional expense to implement further data protection measures.

We depend heavily on our executive officers, principal consultants and others and the loss of their services would materially harm our business.

Our success depends, and will likely continue to depend, upon our ability to hire, retain the services of our current executive officers, principal consultants and others, including Chen Schor, our president and chief executive officer, and Joan Mannick, our chief medical officer. We have entered into employment agreements with Mr. Schor and Dr. Mannick, but they may terminate their employment with us at any time. Although we do not have any reason to believe that we will lose the services of Mr. Schor and Dr. Mannick in the foreseeable future, the loss of their services might impede the achievement of our research, development and commercialization objectives.

Our ability to compete in the biotechnology and pharmaceuticals industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. Our industry has experienced a high rate of turnover of management personnel in recent years. Replacing executive officers or other key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to develop, gain regulatory approval of and commercialize products successfully.

Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these additional key employees on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions.

We rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by other entities and may have commitments under consulting or advisory contracts with those entities that may limit their availability to us. If we are unable to continue to attract and retain highly qualified personnel, our ability to develop and commercialize our product candidates will be limited.

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

We are exposed to the risk that our employees, independent contractors, consultants, collaborators and contract research organizations may engage in fraudulent conduct or other illegal activity. Misconduct by those parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violates:

- FDA regulations or similar regulations of comparable non-U.S. regulatory authorities, including those laws requiring the reporting of true, complete and accurate information to such authorities;
- manufacturing standards;
- federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable non-U.S. regulatory authorities; and
- laws that require the reporting of financial information or data accurately.

Activities subject to these laws also involve the improper use or misrepresentation of information obtained in the course of clinical trials, creating fraudulent data in our preclinical studies or clinical trials or illegal misappropriation of product materials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards 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 have a significant impact on our business and results of operations, including the imposition of civil, criminal and administrative penalties, damages, 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 have a material adverse effect on our ability to operate our business and our results of operations.

We expect to expand our organization, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of regulatory affairs and sales, marketing and distribution, as well as to support our public company operations. To manage these growth activities, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Our management may need to devote a significant amount of its attention to managing these growth activities. Moreover, our expected growth could require us to relocate to a different geographic area of the country. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion or relocation of our operations, retain key employees, or identify, recruit and train additional qualified personnel. Our inability to manage the expansion or relocation of our operations effectively may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could also require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If we are unable to effectively manage our expected growth, our expenses may increase more than expected, our ability to generate revenues could be reduced and we may not be able to implement our business strategy, including the successful commercialization of our product candidates.

Our current operations are concentrated primarily in a single location and any events affecting our headquarters may have material adverse consequences.

Our current operations are primarily located in our principal office in Boston, Massachusetts. Any unplanned event, such as flood, fire, explosion, earthquake, extreme weather condition, medical epidemics, power shortage, telecommunication failure or other natural or manmade accidents or incidents that result in us being unable to fully utilize the office may have a material adverse effect on our ability to operate our business, and have significant negative consequences on our financial and operating conditions. Loss of access to this office may result in increased costs, delays in the

development of our product candidates or interruption of our business operations. As part of our risk management policy, we maintain insurance coverage at levels that we believe are appropriate for our business. However, in the event of an accident or incident at our office, our insurance coverage may not be sufficient to satisfy all of our damages and losses. If our office is unable to operate because of an accident or incident or for any other reason, even for a short period of time, any or all of our research and development programs may be harmed.

Prior to our IPO, which closed on January 30, 2018, we operated as a private company and therefore, have no experience operating as a public company and complying with public company obligations. Complying with these requirements will increase our costs, require additional management resources and qualified accounting and financial personnel, and we may fail to meet all of these obligations.

We will face increased legal, accounting, administrative and other costs and expenses as a public company. Compliance with the Sarbanes-Oxley Act of 2002, the Dodd-Frank Act of 2010 and the rules promulgated thereunder, as well as rules of the SEC and Nasdaq, for example, will result in significant initial cost to us as well as ongoing increases in our legal, audit and financial compliance costs, particularly after we are no longer an "emerging growth company." The Securities Exchange Act of 1934, as amended, or the Exchange Act, requires, among other things, that we file certain periodic reports with respect to our business and financial condition. Our executive officers and other personnel need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance, and require us to incur substantial costs to maintain the same or similar coverage. We expect to incur significant expense and devote substantial management effort toward ensuring compliance with Section 404 of the Sarbanes-Oxley Act of 2002 once we lose our status as an "emerging growth company." We have a limited number of employees performing accounting functions, and we currently do not have an internal audit group. We will need to hire additional accounting and financial staff with appropriate public company experience and technical accounting knowledge, and it may be difficult to recruit and maintain such personnel. Implementing any appropriate changes to our internal controls may require specific compliance training for our directors, officers and employees, entail substantial costs to modify our existing accounting systems, and take a significant period of time to complete. Such changes may not, however, be effective in maintaining the adequacy of our internal controls, and any failure to maintain that adequacy, or consequent inability to produce accurate consolidated financial statements or other reports on a timely basis, could increase our operating costs, could materially impair our ability to operate our business or could lead to accounting fraud or misappropriation of our assets.

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

Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. We currently have a limited number of employees performing our accounting functions, including monitoring and maintaining effective internal control over financial reporting. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404 of the Sarbanes-Oxley Act of 2002, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our consolidated financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our stock.

We will be required to disclose changes made in our internal controls and procedures on a quarterly basis and our management will be required to assess the effectiveness of these controls annually. However, for as long as we are an "emerging growth company" under the JOBS Act, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal controls over financial reporting pursuant to Section 404. We could be an "emerging growth company" for up to five years. An independent assessment of the effectiveness of our internal controls over financial reporting could detect problems that our management's assessment might not. Undetected material weaknesses in our internal controls over financial reporting could lead to financial statement restatements and require us to incur the expense of remediation.

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

Upon completion of our IPO, we became subject to certain reporting requirements of the Exchange Act. Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements or insufficient disclosures due to error or fraud may occur and not be detected.

We have conducted and expect to continue to conduct our operations in jurisdictions outside of the United States, and such foreign operations subject us to additional risks.

A portion of our operations, including our clinical research and development efforts, have been undertaken outside of the United States, and we expect to continue to conduct a portion of our business in foreign countries. For example, we are conducting our ongoing Phase 2b clinical trial across two hemispheres. In addition, we may utilize third party contract organizations, some of which may be located in foreign jurisdictions, for the conduct of our clinical trials, the manufacturing of our product candidates and the commercialization of our product candidates, if approved. Such operations subject us to additional risks related to international business operations, including:

- potentially reduced protection for intellectual property rights;
- price and currency exchange fluctuations;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- difficulties in complying with tax, employment, immigration and labor laws for personnel living or traveling abroad;
- production shortages resulting from any events affecting a product candidate and/or finished drug product supply or manufacturing capabilities abroad;
- business interruptions resulting from geo-political actions, including war and terrorism, or natural disasters, including earthquakes, hurricanes, typhoons, floods and fires; and
- failure to comply with Office of Foreign Asset Control rules and regulations and the Foreign Corrupt Practices Act.

These and other risks may materially adversely affect our ability to conduct our business in international markets.

We may engage in acquisitions that could disrupt our business, cause dilution to our stockholders or reduce our financial resources.

In the future, we may enter into transactions to acquire other businesses, products or technologies. If we do identify suitable candidates, we may not be able to make such acquisitions on favorable terms, or at all. Any acquisitions we make may not strengthen our competitive position, and these transactions may be viewed negatively by customers or investors. We may decide to incur debt in connection with an acquisition or issue our common stock or other equity securities to the stockholders of the acquired company, which would reduce the percentage ownership of our existing stockholders. We could incur losses resulting from undiscovered liabilities of the acquired business that are not covered by the indemnification we may obtain from the seller. In addition, we may not be able to successfully integrate the acquired personnel, technologies

and operations into our existing business in an effective, timely and nondisruptive manner. Acquisitions may also divert management attention from day-to-day responsibilities, increase our expenses and reduce our cash available for operations and other uses. We cannot predict the number, timing or size of future acquisitions or the effect that any such transactions might have on our operating results.

Risks Related to Our Common Stock

An active trading market for our common stock may not develop or be sustainable. If an active trading market does not develop, investors may not be able to resell their shares at or above the purchase price and our ability to raise capital in the future may be impaired.

Our IPO recently closed on January 30, 2018. The initial public offering price for our common stock was determined through negotiations with the underwriters. This price may not reflect the price at which investors in the market will be willing to buy and sell our shares. Although our common stock is listed on The Nasdaq Global Select Market, an active trading market for our shares may never develop or, if developed, be maintained. If an active market for our common stock does not develop or is not maintained, it may be difficult for you to sell shares you purchase without depressing the market price for the shares or at all. An inactive trading market may also impair our ability to raise capital to continue to fund operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

The trading price of our common stock is likely to be highly volatile, which could result in substantial losses for purchasers of our common stock. Securities class action or other litigation involving our company or members of our management team could also substantially harm our business, financial condition and results of operations.

Our stock price is likely to be highly volatile. The stock market in general and the market for smaller pharmaceutical and biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, you may not be able to sell your common stock at or above the purchase price and you may lose some or all of your investment. The market price for our common stock may be influenced by many factors, including:

- the success of existing or new competitive products or technologies;
- regulatory actions with respect to our product candidates or our competitors' products and product candidates;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures, collaborations or capital commitments;
- the timing and results of clinical trials of RTB101 alone or in combination with everolimus and any other product candidates;
- commencement or termination of collaborations for our development programs;
- failure or discontinuation of any of our development programs;
- results of clinical trials of product candidates of our competitors;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our product candidates or clinical development programs;
- the results of our efforts to develop additional product candidates or products;
- actual or anticipated changes in estimates as to financial results or development timelines;

- announcement or expectation of additional financing efforts;
- sales of our common stock by us, our insiders or other stockholders;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in estimates or recommendations by securities analysts, if any, that cover us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- the other factors described in this “Risk Factors” section.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for biopharmaceutical companies, which have experienced significant stock price volatility in recent years.

We are an “emerging growth company,” and the reduced disclosure requirements applicable to emerging growth companies may make our common stock less attractive to investors.

We are an emerging growth company, and, for as long as we continue to be an emerging growth company, we may choose to take advantage of exemptions from various reporting requirements applicable to other public companies but not to “emerging growth companies.” We could remain an “emerging growth company” for up to five years, or until the earliest of (1) the last day of the first fiscal year in which our annual gross revenue exceeds $1.07 billion, (2) the date that we become a “large accelerated filer” as defined in Rule 12b-2 under the Securities Exchange Act of 1934, which would occur if the market value of our common stock that is held by non-affiliates exceeds $700.0 million as of the last business day of our most recently completed second fiscal quarter or (3) the date on which we have issued more than $1.0 billion in non-convertible debt during the preceding three-year period. So long as we remain an “emerging growth company,” we expect to avail ourselves of the exemption from the requirement that our independent registered public accounting firm attest to the effectiveness of our internal control over financial reporting under Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404. When our independent registered public accounting firm is required to undertake an assessment of our internal control over financial reporting, the cost of our compliance with Section 404 will correspondingly increase. Moreover, if we are not able to comply with the requirements of Section 404 applicable to us in a timely manner, or if we or our independent registered public accounting firm identifies deficiencies in our internal control over financial reporting that are deemed to be material weaknesses, the market price of our stock could decline and we could be subject to sanctions or investigations by the SEC or other regulatory authorities, which would require additional financial and management resources.

We will incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, and particularly after we are no longer an “emerging growth company,” we will incur significant legal, accounting and other expenses that we did not incur as a private company, including costs associated with public company reporting requirements. We also anticipate that we will incur costs associated with relatively recently adopted corporate governance requirements, including requirements of the Securities and Exchange Commission, or SEC, and The Nasdaq Global Select Market. We expect these rules and regulations to increase our legal and financial compliance costs and to make some activities more time-consuming and costly. We also expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. As a result, it may be more difficult for us to attract and retain qualified individuals to serve on our board of directors or as executive officers.

We are currently evaluating and monitoring developments with respect to these rules, and we cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice

may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404 of the Sarbanes-Oxley Act, or Section 404, we will be required to furnish a report by our management on our internal control over financial reporting beginning with our second filing of an Annual Report on Form 10-K with the Securities and Exchange Commission, or the SEC, after we become a public company. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our consolidated financial statements.

A significant portion of our total outstanding shares is restricted from immediate resale but may be sold into the market in the near future, which could cause the market price of our common stock to decline significantly, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares of common stock intend to sell shares, could reduce the market price of our common stock. As of March 23, 2018, we had 28,046,315 shares of common stock outstanding. Of these shares, the 6,516,667 shares sold by us in the IPO may be resold in the public market immediately, unless purchased by our affiliates. The remaining 21,529,648 shares are currently restricted under securities laws or as a result of lock-up or other agreements entered into in connection with our IPO, but will be able to be sold in the near term. The representatives of the underwriters may release these stockholders from their lock-up agreements with the underwriters at any time and without notice, which would allow for earlier sales of shares in the public market.

Moreover, holders of an aggregate of 15,870,559 shares of our common stock have rights, subject to conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We have registered and plan to continue to register all shares of common stock that we may issue under our equity compensation plans. Once we register these shares, they can be freely sold in the public market upon issuance and once vested, subject to volume limitations applicable to affiliates and the lock-up agreements. If these additional shares are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

We do not anticipate paying any cash dividends on our capital stock in the foreseeable future. Accordingly, stockholders must rely on capital appreciation, if any, for any return on their investment.

We have never declared nor paid cash dividends on our capital stock. We currently plan to retain all of our future earnings, if any, to finance the operation, development and growth of our business. In addition, the terms of any future debt or credit agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

Concentration of ownership of our common stock among our existing executive officers, directors and principal stockholders may prevent new investors from influencing significant corporate decisions.

Based upon shares outstanding as of March 23, 2018, our executive officers and directors, combined with our stockholders who owned more than 5% of our outstanding common stock and their affiliates, in the aggregate, beneficially own shares representing approximately 83.7% of our common stock. As a result, if these stockholders were to choose to act together, they would be able to control all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would control the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of ownership control may:

- delay, defer or prevent a change in control;
- entrench our management or the board of directors; or
- impede a merger, consolidation, takeover or other business combination involving us that other stockholders may desire.

Some of these persons or entities may have interests different than yours. For example, because many of these stockholders purchased their shares at prices substantially below the price at which shares are currently being sold and have held their shares for a longer period, they may be more interested in selling our company to an acquirer than other investors or they may want us to pursue strategies that deviate from the interests of other stockholders.

Provisions in our corporate charter documents and under Delaware law may prevent or frustrate attempts by our stockholders to change our management or hinder efforts to acquire a controlling interest in us.

Provisions in our corporate charter and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors such that all members of the board are not elected at one time;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from the board;
- establish advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted on at stockholder meetings;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call a special meeting of stockholders;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a “poison pill” that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 66.7% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the General Corporation Law of the State of Delaware, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. This could discourage, delay or prevent someone from acquiring us or merging with us, whether or not it is desired by, or beneficial to, our stockholders. This could also have the effect of discouraging others from making tender offers for our common stock, including transactions that may be in your best interests. These provisions may also prevent changes in our management or limit the price that investors are willing to pay for our stock.

Our restated certificate of incorporation will provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for most legal actions between

us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, employees or agents.

Our restated certificate of incorporation specifies that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for most legal actions involving claims brought against us by stockholders. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our restated certificate of incorporation described above.

We believe this provision benefits us by providing increased consistency in the application of Delaware law by chancellors particularly experienced in resolving corporate disputes, efficient administration of cases on a more expedited schedule relative to other forums and protection against the burdens of multi-forum litigation. However, the provision may have the effect of discouraging lawsuits against our directors, officers, employees and agents as it may limit any stockholder's ability to bring a claim in a judicial forum that such stockholder finds favorable for disputes with us or our directors, officers, employees or agents. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with any applicable action brought against us, a court could find the choice of forum provisions contained in our restated certificate of incorporation to be inapplicable or unenforceable in such action. If a court were to find the choice of forum provision contained in our restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business, financial condition or results of operations.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our share price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that industry or securities analysts publish about us or our business. We do not currently have and may never obtain research coverage by securities and industry analysts. If no or few securities or industry analysts commence coverage of us, or one or more of the analysts who cover us issues an adverse opinion about our company, our stock price would likely decline. If one or more of these analysts ceases research coverage of us or fails to regularly publish reports on us, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

Item 1B. Unresolved Staff Comments.

Not applicable.

Item 2. Properties.

We lease a facility containing our office space, which consists of approximately 4,544 square feet located at 500 Boylston Street, 12th Floor, Boston, Massachusetts. Our lease expires on February 28, 2021.

Item 3. Legal Proceedings.

We are not currently subject to any material legal proceedings.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

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

Our common stock trades on The Nasdaq Global Select Market under the symbol "TORC". Trading of our common stock commenced on January 26, 2018, in connection with our initial public offering, or IPO. Prior to that time, there was no established public trading market for our common stock. As a result, we have not set forth quarterly information with respect to the high and low prices for our common stock for the two most recent fiscal years. The following table sets forth the high and low sale prices per share for our common stock as reported on The Nasdaq Global Select Market for the period indicated:

	Market Price	
	High	Low
First quarter (January 26, 2018 to March 23, 2018)	$ 21.10	$ 11.72

As of March 23, 2018, we had approximately 12 holders of record of our common stock. The actual number of holders of our common stock is greater than this number of record holders and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers or held by other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

We have never declared or paid any cash dividends on our common stock. We currently intend to retain all available funds and any future earnings, if any, to fund the development and growth of our business. We do not expect to pay any cash dividends in the foreseeable future. Any future determination to pay dividends will be made at the discretion of our board of directors and will depend on various factors, including applicable laws, our results of operations, financial condition, future prospects, then applicable contractual restrictions and any other factors deemed relevant by our board of directors. Investors should not purchase our common stock with the expectation of receiving cash dividends.

Recent Sales of Unregistered Securities

Set forth below is information regarding shares of our common stock and shares of our preferred stock issued, and stock options granted, by us during the period covered by this Annual Report on Form 10-K that were not registered under the Securities Act. Included is the consideration, if any, we received for such shares and options and information relating to the section of the Securities Act, or rule of the Securities and Exchange Commission, under which exemption from registration was claimed.

(a) Issuance of Capital Stock

In March 2017, we issued 2,415,300 shares of our common stock to PureTech Health LLC, or PureTech Health, in exchange for its provision of founding strategic medical, clinical and scientific advice, as well as shared administrative support and offices pursuant to a business services, personnel and information management agreement.

In March 2017, we issued and sold an aggregate of 5,434,783 shares of our Series A preferred stock in the first closing of our Series A preferred stock financing to PureTech Health and Novartis Institutes for BioMedical Research, Inc., or NIBR, at a price per share of $1.932. PureTech Health paid approximately $5,017,989 for such Series A shares, and the remaining $482,011 of the purchase price was net settled against invoices paid by PureTech Health on our behalf prior to the closing of our Series A financing and as reimbursement for certain due diligence costs incurred in connection with the financing. The remaining shares were issued in consideration to NIBR for our entry into a license agreement with Novartis International Pharmaceutical Ltd, or Novartis.

In September 2017, we issued and sold 2,329,193 shares of our Series A preferred stock at a price per share of $1.932 in the second closing of our Series A preferred stock financing for a purchase price of approximately $4.5 million.

In October 2017, we issued and sold 7,763,95 shares of our Series A preferred stock at a price per share of $1.932 in the third closing of our Series A preferred stock financing for a purchase price of approximately $15.0 million.

In November 2017, we issued and sold 4,792,716 shares of our Series B preferred stock at a price per share of $8.346 for an aggregate purchase price of approximately $40.0 million.

No underwriters were involved in the foregoing issuances of securities. The securities described in this section (a) of Item 15 were issued to investors in reliance upon the exemption from the registration requirements of the Securities Act, as set forth in Section 4(a)(2) under the Securities Act and Regulation D promulgated thereunder relative to transactions by an issuer not involving any public offering, to the extent an exemption from such registration was required. The recipients of securities in the transactions described above represented that they were accredited investors and were acquiring the securities for their own account for investment purposes only and not with a view to, or for sale in connection with, any distribution thereof and that they could bear the risks of the investment and could hold the securities for an indefinite period of time and appropriate legends were affixed to the instruments representing such securities issued in such transactions.

(b) Stock Option Grants and Option Exercises

During the period covered by this Form 10-K, we granted options to purchase an aggregate of 195,668 shares of common stock, with exercise prices ranging from $0.79 to $9.33 per share, to employees and consultants pursuant to our 2017 stock incentive plan. None of these options have been exercised.

No underwriters were involved in the foregoing issuances of securities. The issuances of stock options described in this paragraph (b) of Item 15 were issued pursuant to written compensatory plans or arrangements with our employees, directors, consultants and advisors, in reliance on the exemption provided by Rule 701 promulgated under the Securities Act, or pursuant to Section 4(a)(2) under the Securities Act, relative to transactions by an issuer not involving any public offering, to the extent an exemption from such registration was required. All recipients either received adequate information about us or had access, through employment or other relationships, to such information.

Purchase of Equity Securities

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

Use of Proceeds from Registered Securities

In January 2018, we completed our IPO pursuant to a registration statement on Form S-1 (File No. 333-222273), which was filed on December 29, 2018 and amended subsequently and declared effective on January 25, 2018. In the IPO, we issued and sold 6,516,667 shares of common stock (inclusive of 850,000 shares of common stock sold by us pursuant to the full exercise of an overallotment option granted to the underwriters in connection with the offering) at a public offering price of $15.00 per share, for aggregate gross proceeds of $97.8 million. The managing underwriters for the IPO were Merrill Lynch, Pierce, Fenner & Smith Incorporated, Leerink Partners LLC and Evercore ISI. The IPO commenced on January 25, 2018 and did not terminate until the sale of all of the shares offered.

The aggregate proceeds received by the Company from the IPO were $89.4 million, net of underwriting discounts and commissions and estimated offering expenses payable by us. No offering expenses were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning 10.0% or more of any class of our equity securities or to any other affiliates. Because the closing of our IPO occurred on January 30, 2018, as of December 31, 2017, we had not yet received the net proceeds from the sale of shares of common stock in our IPO and therefore had used none of the proceeds as of December 31, 2017.

Information related to use of proceeds from registered securities is incorporated herein by reference to the “Use of Proceeds” section of the Company’s final prospectus related to the IPO. There has been no material change in the planned use of proceeds from our IPO as described in our final prospectus.

Stock Performance Graph

We have elected not to include a performance graph in this Annual Report on Form 10-K because the period between the date that our common stock began trading on the Nasdaq Global Select Market and the end of our most recently completed fiscal year is 30 days or less.

Item 6. Selected Financial Data.

The following tables summarize our financial data as of the dates and for the periods indicated. The selected consolidated statements of operations data for the year ended December 31, 2017 and the period from July 5, 2016 (inception) through December 31, 2016 and the consolidated balance sheet data as of December 31, 2017 and 2016 have been

derived from our audited consolidated financial statements included elsewhere in this Annual Report on Form 10-K. Our historical results from any prior period are not necessarily indicative of results to be expected in any future period, and our interim period results are not necessarily indicative of results to be expected for a full year or any other interim period. The selected financial data below should be read in conjunction with the section entitled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and related notes included elsewhere in this Annual Report on Form 10-K.

	Year ended December 31, 2017	July 5, 2016 (inception) through December 31, 2016
	(In thousands, except share and per share data)	
Consolidated Statements of Operations Data:		
Operating expenses:		
Research and development	$ 16,839	$ —
General and administrative	2,043	1
Total operating expenses	18,882	1
Loss from operations	(18,882)	(1)
Other expense, net	(14,896)	—
Net loss	$ (33,778)	$ (1)
Net loss per share, basic and diluted(1)	$ (8.42)	$ (0.00)
Weighted-average common shares used in computing net loss per share, basic and diluted(1)	4,009,513	1,978,137

(1) See Notes 2 and 12 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K for an explanation of the calculation of our basic and diluted net loss per share and the weighted-average common shares used in computing basic and diluted net loss per share.

	As of December 31,	
	2017	2016
	(In thousands)	
Consolidated Balance Sheet Data:		
Cash and cash equivalents	$ 53,349	$ —
Working capital(1)	49,652	—
Total assets	55,193	—
Total liabilities	5,502	—
Redeemable convertible preferred stock	81,620	—
Total stockholders' (deficit) equity	(31,929)	—

(1) We define working capital as current assets less current liabilities.

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

You should read the following discussion and analysis of our financial condition and results of operations together with the section entitled "Selected Financial Data" and our consolidated financial statements and related notes included elsewhere in this Annual Report on Form 10-K. This discussion and other parts of this Annual Report on Form 10-K contain forward-looking statements that involve risks and uncertainties, such as our plans, objectives, expectations, intentions and beliefs. Our actual results could differ materially from those discussed in these forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those identified below and those discussed in the section entitled "Risk Factors" included elsewhere in this Annual Report on Form 10-K.

Overview

We are a clinical-stage biopharmaceutical company focused on the development and commercialization of novel therapeutics for the treatment of aging-related diseases. Our lead program has demonstrated in several clinical trials, including a randomized, placebo-controlled trial, the potential to treat multiple diseases of aging for which there are no approved therapies. The decline in immune function that occurs during aging, or immunosenescence, increases susceptibility to a variety of diseases, including respiratory tract infections, or RTIs, that significantly contribute to morbidity and mortality in the elderly. Our approach focuses on the mechanistic target of rapamycin, or mTOR, pathway, an evolutionarily conserved pathway that regulates aging, and specifically on selective inhibition of the target of rapamycin complex 1, or TORC1. Our initial focus is on the development of RTB101, an orally administered, small molecule, potent TORC1 inhibitor, alone and in combination with other mTOR inhibitors such as everolimus—as a first-in-class immunotherapy program designed to improve immune function and thereby reduce the incidence of RTIs in the elderly regardless of the causative pathogen. We licensed the worldwide rights to our TORC1 program, including RTB101 alone or in combination with everolimus or other mTOR inhibitors, from Novartis International Pharmaceutical Ltd., or Novartis, in March 2017. We are evaluating RTB101 alone and in combination with everolimus in a Phase 2b clinical trial for the reduction of RTI incidence in the elderly and expect to report top-line data from this trial in the second half of 2018.

Since our inception in July 2016, we have devoted substantially all of our resources to: identifying, acquiring, and developing our product candidate portfolio; organizing and staffing our company; raising capital; developing manufacturing capabilities; conducting clinical trials; and providing general and administrative support for these operations. To date, we have primarily financed our operations through the issuance and sale of our redeemable convertible preferred stock and our initial public offering of our common stock, or IPO. In January 2018, we closed our IPO. We received aggregate net proceeds from the IPO of approximately $89.4 million, after deducting underwriting discounts and commissions and other offering expenses payable by us.

We have never generated revenue and have incurred significant net losses since inception. Our net losses were $1,000 and $33.8 million, for the period from July 5, 2016 (inception) through December 31, 2016, and for the year ended December 31, 2017, respectively. As of December 31, 2017, we had an accumulated deficit of $33.8 million. Our net losses may fluctuate significantly from quarter to quarter and year to year. We expect to incur significant expenses and increasing operating losses for the foreseeable future. We anticipate that our expenses will increase substantially as we:

- invest significantly to further develop and seek regulatory approval for RTB101 alone or in combination with everolimus, including to continue our ongoing Phase 2b clinical trial;
- expand our pipeline of potential product candidates, including the initiation of at least one additional proof of concept trial in an additional indication;
- require the manufacture of larger quantities of our product candidates for clinical development and potentially commercialization;
- hire additional clinical, scientific, management and administrative personnel;
- ultimately establish a sales, marketing and distribution infrastructure or collaborate with third parties to commercialize any drugs for which we may obtain regulatory approval;
- maintain, expand and protect our intellectual property portfolio;
- acquire or in-license other assets and technologies; and

- add additional operational, financial and management information systems and processes to support our ongoing development efforts, any future manufacturing or commercialization efforts and our transition to operating as a public company.

We believe that our available funds, including the net proceeds of $89.4 million we received in our IPO, will be sufficient to fund our operations through 2020. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. We do not expect to generate revenue from product sales unless and until we successfully complete development and obtain regulatory approval for a product candidate or enter into collaborative agreements with third parties, which we expect will take a number of years and the outcome of which is subject to significant uncertainty. Additionally, we currently use third parties such as contract research organizations, or CROs, and contract manufacturing organizations, or CMOs, to carry out our preclinical and clinical development activities and we do not yet have a sales organization. If we obtain regulatory approval for our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. To fund our current and future operating plans, we will need additional capital, which we may obtain through one or more equity offerings, debt financings or other third-party funding, including potential strategic alliances and licensing or collaboration arrangements. We may, however, be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. Our failure to raise capital or enter into such other arrangements as and when needed would have a negative impact on our financial condition and our ability to develop our current product candidates, or any additional product candidates, if developed. The amount and timing of our future funding requirements will depend on many factors, including the pace and results of our preclinical and clinical development efforts. We cannot assure you that we will ever be profitable or generate positive cash flow from operating activities.

Novartis License Agreement

On March 23, 2017, we entered into a license agreement with Novartis, pursuant to which we were granted an exclusive, field-restricted, worldwide license to certain intellectual property rights owned or controlled by Novartis, including patents, patent applications, proprietary information, know-how and other intellectual property, to develop, commercialize and sell one or more therapeutic products comprising RTB101 or RTB101 and everolimus in a fixed dose combination. Under the license agreement, we have been licensed a patent portfolio of ten patent families directed to composition of matter of RTB101 and its salts, formulations of everolimus and methods of using RTB101 and everolimus to enhance the immune response among others. The exclusive field under the license agreement is for the treatment, prevention and diagnosis of diseases and other conditions in all indications in humans and animals.

As initial consideration for the license, we issued Novartis Institutes for Biomedical Research, Inc., or NIBR, 2,587,992 shares of our Series A Preferred Stock.

The agreement may be terminated by either party upon a material breach of obligation by the other party that is not cured with 60 days after written notice. We may terminate the agreement in its entirety or on a product-by-product or country-by-country basis with or without cause with 60 days' prior written notice.

Novartis may terminate the portion of the agreement related to everolimus if we fail to use commercially reasonable efforts to research, develop and commercialize a product utilizing everolimus for a period of three years. Novartis may terminate the license agreement upon our bankruptcy, insolvency, dissolution or winding up.

As additional consideration for the license, we are required to pay up to an aggregate of $4.3 million upon the satisfaction of clinical milestones, up to an aggregate of $24 million upon the satisfaction of regulatory milestones for the first indication approved, and up to an aggregate of $18 million upon the satisfaction of regulatory milestones for the second indication approved. In addition, we are required to pay up to an aggregate of $125 million upon the satisfaction of commercial milestones, based on the amount of annual net sales. We are also required to pay tiered royalties ranging from a mid-single digit percentage to a low-teen digit percentage on annual net sales of products. These royalty obligations last on a product-by-product and country-by-country basis until the latest of (i) the expiration of the last valid claim of a Novartis patent covering a subject product, (ii) the expiration of any regulatory exclusivity for the subject product in a country, or (iii) the 10th anniversary of the first commercial sale in the country, and are subject to a reduction after the expiration of the last valid claim of a Novartis patent or the introduction of a generic equivalent of a product in a country. In addition, if we sublicense the rights under the license agreement, we are required to pay a certain percentage of the sublicense revenue to Novartis. Novartis will no longer be entitled to sublicense revenue following the last visit of the 400th subject in any human clinical trial conducted by us or a sublicensee of ours, which we expect to occur by the end of our ongoing Phase 2b clinical trial.

Milestone payments to Novartis will be recorded as research and development expenses in our consolidated statements of operations once achievement of each associated milestone has occurred or the achievement is considered probable. In May 2017, we initiated a Phase 2b clinical trial for a first indication, triggering the first milestone payment under the agreement. Accordingly, we paid the related $0.3 million payment in May 2017. As of December 31, 2017, none of the remaining development milestones, regulatory milestones, sales milestones, or royalties had been reached or were probable of achievement. We also enter into contracts in the normal course of business with various third parties for preclinical research studies, clinical trials, testing and other services. These contracts generally provide for termination upon notice, and therefore we believe that our noncancelable obligations under these agreements are not material.

Financial Operations Overview

Revenue

We have not generated any revenue from the sale of our products, and we do not expect to generate any revenue unless and until we obtain regulatory approval of and commercialize RTB101, alone or in combination with everolimus.

Operating Expenses

Research and Development

Research and development expenses consist primarily of costs incurred for the development of our product candidates, which include:

- personnel costs, which include salaries, benefits and stock-based compensation expense;
- expenses incurred under agreements with consultants, third-party contract organizations and investigative clinical trial sites that conduct research and development activities on our behalf;
- costs related to production of preclinical and clinical materials, including fees paid to contract manufacturers;
- laboratory and vendor expenses related to the execution of preclinical studies and clinical trials; and
- lab supplies and equipment used for internal research and development activities.

We have not provided program costs since inception because historically we have not tracked or recorded our research and development expenses on a program-by-program basis. We use our personnel and infrastructure resources across multiple research and development programs directed toward developing our TORC1 program and for identifying and developing product candidates. We manage certain activities such as contract research and manufacturing of RTB101 alone or in combination with everolimus and our discovery programs through our third-party vendors, and do not track the costs of these activities on a program-by-program basis.

We expense all research and development costs in the periods in which they are incurred. Costs for certain development activities are recognized based on an evaluation of the progress to completion of specific tasks using information and data provided to us by our vendors and third-party service providers.

We expect our research and development expenses to increase substantially for the foreseeable future as we continue to invest in research and development activities related to developing our product candidates, including investments in manufacturing, as our programs advance into later stages of development and we continue to conduct clinical trials. The process of conducting the necessary clinical research to obtain regulatory approval is costly and time-consuming, and the successful development of our product candidates is highly uncertain. As a result, we are unable to determine the duration and completion costs of our research and development projects or when and to what extent we will generate revenue from the commercialization and sale of any of our product candidates.

Because of the numerous risks and uncertainties associated with product development, we cannot determine with certainty the duration and completion costs of the current or future preclinical studies and clinical trials or if, when, or to what extent we will generate revenues from the commercialization and sale of our product candidates. We may never succeed

in achieving regulatory approval for our product candidates. The duration, costs and timing of preclinical studies and clinical trials and development of our product candidates will depend on a variety of factors, including:

- successful completion of preclinical studies and Investigational New Drug-enabling studies;
- successful enrollment in, and completion of, clinical trials;
- receipt of regulatory approvals from applicable regulatory authorities;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and non-patent exclusivity;
- launching commercial sales of our product candidates, if and when approved, whether alone or in collaboration with others;
- acceptance of our product candidates, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies and treatment options;
- a continued acceptable safety profile following approval;
- enforcing and defending intellectual property and proprietary rights and claims; and
- achieving desirable medicinal properties for the intended indications.

A change in the outcome of any of these factors could mean a significant change in the costs and timing associated with the development of our current and future preclinical and clinical product candidates. For example, if the FDA, or another regulatory authority were to require us to conduct clinical trials beyond those that we currently anticipate will be required for the completion of clinical development, or if we experience significant delays in execution of or enrollment in any of our preclinical studies or clinical trials, we could be required to expend significant additional financial resources and time on the completion of preclinical and clinical development. We expect our research and development expenses to increase for the foreseeable future as we continue the development of product candidates.

General and Administrative

General and administrative expenses consist primarily of personnel costs, costs related to maintenance and filing of intellectual property, depreciation expense and other expenses for outside professional services, including legal, human resources, audit and accounting services. Personnel costs consist of salaries, benefits and stock-based compensation expense. We expect our general and administrative expenses to increase for the foreseeable future due to anticipated increases in headcount to advance our product candidates and as a result of operating as a public company, including expenses related to compliance with the rules and regulations of the Securities and Exchange Commission, The Nasdaq Global Select Market, additional insurance expenses, investor relations activities and other administration and professional services.

Other Income, Net

Other income, net, consists of non-cash changes in fair value of the tranche rights liability associated with the redeemable convertible preferred stock.

Critical Accounting Polices and Estimates

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

Accrued Research and Development Costs

We accrue for estimated costs of research and development activities conducted by third-party service providers, which include the conduct of preclinical studies, clinical trials, and contract manufacturing activities. We record the estimated costs of research and development activities based upon the estimated amount of services provided, and include these costs in accrued liabilities in our consolidated balance sheets and within research and development expenses in our consolidated statements of operations. These costs are a significant component of our research and development expenses. We estimate the amount of work completed by third-party service providers through discussions with internal personnel and external service providers as to the progress or stage of completion of the services and the agreed-upon fee to be paid for such services. The majority of our service providers invoice in arrears for services performed, on a pre-determined schedule or when contractual milestones are met;, however, some require advanced payments. We make significant judgments and estimates in determining the accrued balance in each reporting period based on the facts and circumstances known at that time. As actual costs become known, we adjust our accrued estimates. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed, the number of patients enrolled and the rate of patient enrollment may vary from our estimates and could result in us reporting amounts that are too high or too low in any particular period. Our accrued expenses are dependent, in part, upon the receipt of timely and accurate reporting from CROs, CMOs and other third-party service providers. To date, there have been no material differences from our accrued expenses to actual expenses.

Research and Development Costs

Research and development costs are expensed as incurred and consist of personnel costs, lab supplies and other costs, as well as fees paid to third parties to conduct research and development activities on our behalf.

Amounts incurred in connection with license agreements are also included in research and development expenses. We record payments made to outside vendors for services performed or goods being delivered for use in research and development activities as either prepaid expenses or accrued expenses, depending on the timing of when services are performed or goods are delivered.

Determination of Fair Value of Common and Preferred Shares and Tranche Rights Liabilities

Prior to the completion of our IPO, we were required to estimate the fair value of our common stock underlying our stock-based awards when performing the fair value calculations using the Black-Scholes option pricing model. The estimated fair value of our common and preferred shares has been determined by the board of directors as of the grant date, with input from management, considering our most recently available third-party valuations of common shares and preferred shares and the board of directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent valuation through the date of the grant. These third party valuations were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*, or the Practice Aid. Our common and preferred share valuations were prepared using either an option-pricing method, or OPM, or a probability-weighted expected return method, or PWERM, which uses a combination of market approaches and an income approach to estimate our enterprise value. The OPM treats common securities and preferred securities as call options on the total equity value of a company, with exercise prices based on the value thresholds at which the allocation among the various holders of a company's securities changes. Under this method, the common and preferred shares have value only if the funds available for distribution to stockholders are expected to exceed the value of the preferred security liquidation preference at the time of the liquidity event, such as a strategic sale or a merger. The PWERM is a

scenario-based methodology that estimates the fair value of common and preferred shares based upon an analysis of future values for the enterprise, assuming various outcomes. The common and preferred share values are based on the probability-weighted present value of expected future investment returns considering each of the possible outcomes available as well as the rights of each class of common and preferred securities. The future value of the common and preferred shares under each outcome is discounted back to the valuation date at an appropriate risk-adjusted discount rate and probability weighted to arrive at an indication of value for the common and preferred shares. The estimated fair value of the tranche rights was determined using the difference between the total purchase price of our preferred stock and the total fair value of the preferred stock using a risk-adjusted forward contract model.

Stock-Based Compensation Expense

We recognize equity-based compensation expense for awards of equity instruments to employees and non-employees based on the grant date fair value of those awards in accordance with the Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, Topic 718, *Stock Compensation*, or ASC 718. ASC 718 requires all equity-based compensation awards to employees and non-employee directors, including grants of restricted shares and stock options, to be recognized as expense in the consolidated statements of operations based on their grant date fair values. We estimate the fair value of stock options using the Black-Scholes option pricing model. We use the value of our common stock to determine the fair value of restricted shares.

We account for restricted stock and common stock options issued to non-employees under FASB ASC Topic 505-50, *Equity-Based Payments to Non-Employees*, or ASC 505-50. As such, the value of such options is periodically remeasured and income or expense is recognized over their vesting terms. Compensation cost related to awards with service-based vesting schedules is recognized using the straight-line method. We determine the fair value of the restricted stock and common stock granted to non-employees as either the fair value of the consideration received or the fair value of the equity instruments issued.

The Black-Scholes option pricing model requires the input of certain subjective assumptions, including (i) the expected volatility, (ii) the expected term of the award, (iii) the risk-free interest rate and (iv) the expected dividend yield. Due to the lack of a public market for the trading of our common stock and a lack of company-specific historical and implied volatility data, we have based our estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. The historical volatility is calculated based on a period of time commensurate with the expected term assumption. The group of representative companies has characteristics similar to us, including stage of product development and focus on the life science industry. We use the simplified method, which is the average of the final vesting tranche date and the contractual term, to calculate the expected term for options granted to employees as we do not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. For options granted to non-employees, we utilize the contractual term of the arrangement as the basis for the expected term assumption. The risk-free interest rate is based on a treasury instrument whose term is consistent with the expected term of the stock options. We use an assumed dividend yield of zero as we have never paid dividends and have no current plans to pay any dividends on our common stock.

The following table presents the assumptions used to estimate the fair value of options granted during the year ended December 31, 2017:

	Year Ended December 31, 2017
Employees:	
Fair value of common stock	$0.79 - $9.33
Expected term (in years)	5.9-6.2
Expected volatility	74.4%-74.5%
Risk-free interest rate	1.9%-2.2%
Expected dividend yield	0.0%
Non-employees:	
Fair value of common stock	$0.79 - $1.00
Expected term (in years)	10.0
Expected volatility	74.6%-76.9%
Risk-free interest rate	2.3%
Expected dividend yield	0.0%

There were no stock options granted during the period from July 5, 2016 (inception) to December 31, 2016.

For the year ended December 31, 2017 and the period from July 5, 2016 (inception) through December 31, 2016, stock-based compensation expense was $0.5 million and $0, respectively. As of December 31, 2017, we had $1.9 million of total unrecognized stock-based compensation expense, which we expect to recognize over a weighted-average period of 3.14 years.

The following table presents the grant dates of common shares, stock options, and awards that we granted from July 5, 2016 (inception) through December 31, 2017 along with the corresponding purchase or exercise price for each grant and our estimate of the fair value per share of our common stock on each grant date, which we utilized to calculate stock-based compensation expense:

Grant Date	Type of Award	Number of Shares	Purchase or Exercise Price per Share	Estimate of Common Stock Fair Value per Share on Grant Date
7/11/2016	Restricted common shares	3,772,726	$ 0.0001	$ 0.0001
3/1/2017	Common shares	1,886,363	$ 0.0001	$ 0.0001
6/12/2017	Options	101,948	$ 0.79	$ 0.62
9/14/2017	Options	9,372	$ 1.00	$ 0.78
12/5/2017	Options	84,349	$ 9.33	$ 9.33

Determination of the Fair Value of Common Stock on Grant Dates

Prior to the completion of our IPO, we were required to estimate the fair value of our common stock underlying our stock-based awards when performing the fair value calculations using the Black-Scholes option pricing model. The fair values of the shares of common stock underlying our share-based awards were estimated on each grant date by our board of directors. The restricted common shares were granted to non-employees and subsequently were marked to market at each reporting date. On April 4, 2017, the non-employees became employees of our company and the fair value of the remaining unvested shares was fixed at $0.79 per share. In order to determine the fair value of our common stock our board of directors considered, among other things, contemporaneous valuations of our common stock prepared by an independent third-party valuation specialist in accordance with the guidance provide by the Practice Aid.

Given the absence of a public trading market for our common stock prior to the IPO, our board of directors exercised their judgment and considered a number of objective and subjective factors to determine the best estimate of the fair value of our common stock, including our stage of development; progress of our research and development efforts; the rights, preferences and privileges of our preferred stock relative to those of our common stock; equity market conditions affecting comparable public companies; the lack of marketability of our common stock; and valuations obtained from issuance of our preferred stock to unrelated parties.

We performed common stock valuations, with the assistance of an independent third-party valuation specialist, as of March 23, 2017, September 8, 2017, November 30, 2017 and December 31, 2017, which resulted in valuations of our common stock of $0.79, $1.00, $9.33 and $13.17, respectively. In conducting the valuations, the independent third-party valuation specialist considered all objective and subjective factors that it believed to be relevant for each valuation conducted in accordance with the Practice Aid, including our best estimate of our business condition, prospects and operating performance at each valuation date. Other significant factors included:

- the prices of our preferred stock sold to outside investors in arm’s length transactions, and the rights, preferences and privileges of our preferred stock as compared to those of our common stock, including the liquidation preferences of our preferred stock;
- our stage of development and business strategy and the material risks related to our business and industry;
- the valuation of publicly traded companies in the life sciences and biotechnology sectors, as well as recently completed mergers and acquisitions of guideline companies;

- our results of operations and financial position;
- the composition of, and changes to, our management team and board of directors;
- the lack of liquidity of our common stock;
- any external market conditions affecting the life sciences and biotechnology industry sectors;
- the likelihood of achieving a liquidity event for the holders of our common stock and stock options, such as an IPO or a sale of our company, given prevailing market conditions; and
- the state of the IPO market for similarly situated privately held life sciences companies.

The dates of our contemporaneous valuations have not always coincided with the dates of our stock option grants. In determining the exercise prices of the stock options set forth in the table above, our board of directors considered, among other things, the most recent valuation of our common stock and their assessment of additional objective and subjective factors that were relevant as of the grant dates. The additional factors considered when determining whether any changes in the fair value of our common stock had occurred between the most recent valuation and the grant dates included our stage of research and development, our operating and financial performance and current business conditions.

The estimates of fair value of our common stock are highly complex and subjective. There are significant judgments and estimates inherent in the determination of the fair value of our common stock. These judgments and estimates include assumptions regarding our future operating performance, the time to completing an IPO or other liquidity event, the related valuations associated with these events, and the determinations of the appropriate valuation methods at each valuation date. The assumptions underlying these valuations represent management's best estimates, which involve inherent uncertainties and the application of management judgment. If we had made different assumptions, our stock-based compensation expense, net loss and net loss per share applicable to common stockholders could have been materially different.

Results of Operations

Comparison of the Year Ended December 31, 2017 and the period from July 5, 2016 (Inception) through December 31, 2016 and the Year Ended December 31, 2017

	Year Ended December 31, 2017	July 5, 2016 (inception) through December 31, 2016
	(In thousands)	
Operating expenses:		
Research and development	$ 16,839	$ —
General and administrative	2,043	1
Total operating expenses	18,882	1
Loss from operations	(18,882)	(1)
Other expense, net	(14,896)	—
Net loss	$ (33,778)	$ (1)

Research and Development

Research and development expenses increased to $16.8 million for the year ended December 31, 2017, and were primarily attributable to $3.9 million of costs associated with our license agreement, including the license of the intellectual property in exchange for Series A preferred stock, $1.3 million of costs related to contract research and supplies, $10.0 million of costs related to clinical trials, including the ongoing Phase 2b clinical trial, $0.6 million of costs related to external consulting incurred to supplement our research and development personnel, and $1.0 million of personnel costs. We did not have any research and development expenses for the period from July 5, 2016 (inception) through December 31, 2016, as our primary operations did not commence until March 23, 2017, when we acquired our license to develop, make, use, and sell products incorporating RTB101 alone or in combination with everolimus.

General and Administrative

General and administrative expenses increased to $2.0 million for the year ended December 31, 2017, and were primarily attributable to $1.0 million of personnel, and $1.0 million of professional services fees, including costs related to intellectual property, legal and filing costs, accounting costs, and external consulting costs incurred to supplement our personnel. General and administrative expenses were $1,000 for the period from July 5, 2016 (inception) through December 31, 2016, and consisted entirely of registration and filing fees related to our incorporation.

Other Expense, Net

Other expense, net was $14.9 million for the year ended December 31, 2017, and entirely consisted of the change in fair value of our tranche liability related to our redeemable convertible preferred stock. Other expense, net was $0 for the period from July 5, 2016 (inception) through December 31, 2016.

Liquidity, Capital Resources and Plan of Operations

Since inception through December 31, 2017, our operations have been financed solely by net proceeds of $64.9 million from the issuance and sale of shares of our redeemable convertible preferred stock. As of December 31, 2017, we had $53.3 million in cash and cash equivalents and an accumulated deficit of $33.8 million. In January 2018, we closed our IPO. We received aggregate net proceeds from the IPO of approximately $89.4 million, after deducting underwriting discounts and commissions and other offering expenses payable by us.

Our primary use of cash has been to fund operating expenses, which consist of research and development and general and administrative expenditures. Cash used to fund operating expenses is impacted by the timing of when we pay these expenses, as reflected in the change in our outstanding accounts payable and accrued expenses.

Based upon our current operating plan, we believe that our existing cash and cash equivalents, together with the net proceeds from our IPO will enable us to fund our operating expenses and capital expenditure requirements through 2020, including the completion of our ongoing Phase 2b clinical trial of RTB101 alone or in combination with everolimus, the completion of a subsequent pivotal Phase 3 clinical program, assuming a successful outcome in our Phase 2b clinical trial of RTB101 alone or in combination with everolimus, and the filing of an NDA with the FDA, assuming a successful outcome in our Phase 3 clinical program. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. We will continue to require additional financing to advance our current product candidate through clinical development, to develop, acquire or in-license other potential product candidates and to fund operations for the foreseeable future. Furthermore, with the closing of our IPO, we have begun to incur additional costs associated with operating as a public company. Accordingly, we will continue to seek funds through equity or debt financings, collaborative or other arrangements, or through other sources of financing. Adequate additional funding may not be available to us on acceptable terms, or at all. Any failure to raise capital as and when needed could have a negative impact on our financial condition and on our ability to pursue our business plans and strategies.

Further, our operating plans may change, and we may need additional funds to meet operational needs and capital requirements for clinical trials and other research and development activities. We currently have no credit facility or committed sources of capital. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenditures associated with our current and anticipated product development programs.

If we need to raise additional capital to fund our operations, funding may not be available to us on acceptable terms, or at all. If we are unable to obtain adequate financing when needed, we may have to delay, reduce the scope of or suspend one or more of our clinical trials, research and development programs or commercialization efforts. We may seek to raise any necessary additional capital through a combination of public or private equity offerings, debt financings, and collaborations or licensing arrangements. If we do raise additional capital through public or private equity offerings, the ownership interest of our existing stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights. If we raise additional capital through debt financing, we may be subject to covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If additional funding is required, there can be no assurance that additional funds will be available to us on acceptable terms on a timely basis, if at all. If we are unable to raise capital, we will need to curtail planned activities to reduce costs. Doing so will likely have an unfavorable effect on our ability to execute our business plans.

The following table summarizes our cash flows for the periods indicated:

	Year Ended December 31, 2017	July 5, 2016 (inception) through December 31, 2016
	(In thousands)	
Net cash used in operating activities	$ (10,985)	$ —
Net cash used in investing activities	(44)	—
Net cash provided by financing activities	64,378	—
Net increase in cash	$ 53,349	$ —

Cash Flows from Operating Activities

Cash used in operating activities for year ended December 31, 2017 was $11.0 million, consisting of a net loss of $33.8 million adjusted for noncash items including the loss resulting from the change in fair value of the tranche liability of $14.9 million, stock-based compensation expense of $0.5 million and expense related to the acquisition of intellectual property of $3.2 million. The change in our net operating assets and liabilities were due primarily to an increase in accounts payable of $1.4 million as a result of payment timing and an increase in accrued liabilities of $3.7 million primarily due to increased clinical activities, which were partially offset by an increase in prepaid expenses and other current assets of $0.9 million due to prepayments for our research and development activities. No cash was used in operating activities for the period from July 5, 2016 (inception) through December 31, 2016.

Cash Flows from Investing Activities

Cash used in investing activities for the year ended December 31, 2017 was $44,000 and consisted of the purchases of property and equipment. No cash was used in investing activities for the period from July 5, 2016 (inception) through December 31, 2016.

Cash Flows from Financing Activities

Cash provided by financing activities for the year ended December 31, 2017 was $64.4 million primarily from the issuance of redeemable convertible preferred stock partially offset by costs incurred in connection with the IPO. No cash was provided by financing activities for the period from July 5, 2016 (inception) through December 31, 2016.

Contractual Obligations and Other Commitments

The following table summarizes our outstanding contractual obligations as of payment due date by period at December 31, 2017.

Total	Less than 1 Year	1 to 3 Years	3 to 5 Years	More than 5 Years
$ —	$ —	$ —	$ —	$ —

In March 2017, we entered into a license Agreement with Novartis. See "—Overview—Novartis License Agreement." Amounts owed under this license agreement are not included in the table above as they were considered a contingent payment as of December 31, 2017.

In January 2018, we entered into a multi-year agreement to lease office space in Boston, Massachusetts under an operating lease agreement. Our minimum rent commitment under the lease totals approximately $0.7 million. Payments under the contract are expected to commence in March 2018.

We enter into contracts in the normal course of business with CROs and CMOs to assist in the performance of our research and development activities and other services and products for operating purposes. These contracts generally provide for termination upon notice, and therefore are cancelable contracts and not included in the table of contractual obligations and commitments.

Net Operating Loss Carryforwards

As of December 31, 2017, we had federal and state net operating loss carryforwards of $14.5 million and $14.4 million, respectively, which begin to expire in various amounts in 2036. As of December 31, 2017, we also had federal research and development tax credit carryforwards of $0.2 million, which begin to expire in 2037.

On December 22, 2017, President Trump signed into law the "Tax Cuts and Jobs Act", or TCJA, that significantly reforms the Internal Revenue Code of 1986, as amended, or the Code. The TCJA, among other things, includes changes to U.S. federal tax rates, imposes significant additional limitations on the deductibility or interest and net operating loss carryforwards, allows for the expensing of capital expenditures, and puts into effect the migration from a "worldwide" system of taxation to a territorial system. Our net deferred tax assets and liabilities will be revalued at the newly enacted U.S. corporate rate. We do not expect to recognize any tax expense in the year of enactment as our net deferred tax assets have a full valuation allowance recorded. We continue to examine the impact this tax reform legislation may have on our business.

In general, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, a corporation that undergoes an "ownership change" is subject to limitations on its ability to utilize its pre-change net operating losses or tax credits, or NOLs or credits, to offset future taxable income or taxes. For these purposes, an ownership change generally occurs where the aggregate stock 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 specified testing period. Our existing NOLs or credits may be subject to limitations arising from previous ownership changes, and if we undergo an ownership change in connection with or after our IPO, our ability to utilize NOLs or credits could be further limited by Sections 382 and 383 of the Code. In addition, future changes in our stock ownership, many of which are outside of our control, could result in an ownership change under Sections 382 and 383 of the Code. Our NOLs or credits may also be impaired under state law. Accordingly, we may not be able to utilize a material portion of our NOLs or credits. We have not completed a study to determine whether our IPO, our most recent private placement of our Series B preferred stock and other transactions that have occurred over the past three years may have triggered an ownership change limitation. If we determine that an ownership change has occurred and our ability to use our historical NOLs or credits is materially limited, it would harm our future operating results by effectively increasing our future tax obligations. We have not performed an ownership change analysis.

Furthermore, our ability to utilize our NOLs or credits is conditioned upon our attaining profitability and generating U. S. federal and state taxable income. As described above under "Risk Factors—Risks Related to our Financial Position and Need for Additional Capital," we have incurred significant net losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future; and therefore, we do not know whether or when we will generate the U.S. federal or state taxable income necessary to utilize our NOL or credit carryforwards that are subject to limitation by Sections 382 and 383 of the Code.

Off-Balance Sheet Arrangements

We have not entered into any off-balance sheet arrangements and do not have any holdings in variable interest entities.

Quantitative and Qualitative Disclosures about Market Risk

We are exposed to market risks in the ordinary course of our business. We had cash and cash equivalents as of December 31, 2017 of $53.3 million, primarily money market mutual funds consisting of U.S. government-backed securities. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments are in short-term securities. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our portfolio.

JOBS Act Accounting Election

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. Under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act until such time as those standards apply to private companies. We are considering whether to "opt out" of this provision and thereby comply with new or revised accounting standards as required

when they are adopted. If we do decide to "opt out," this decision to "opt out" of the extended transition period under the JOBS Act is irrevocable.

We are in the process of evaluating the benefits of relying on other exemptions and reduced reporting requirements under the JOBS Act. Subject to certain conditions, as an emerging growth company, we may rely on certain of these exemptions, including without limitation, providing an auditor's attestation report on our system of internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act. We would cease to be an emerging growth company upon the earliest of: (1) the last day of the fiscal year ending after the fifth anniversary of our initial public offering; (2) the last day of the fiscal year in which we have more than $1.07 billion in annual revenue; (3) the date we qualify as a "large accelerated filer," with at least $700.0 million of equity securities held by non-affiliates; or (4) the issuance, in any three-year period, by our company of more than $1.0 billion in non-convertible debt securities held by non-affiliates.

Recently Issued and Adopted Accounting Pronouncements

In August 2014, the FASB issued ASU 2014-15, *Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern*, or ASU 2014-15. ASU 2014-15 requires management to evaluate relevant conditions, events, and certain management plans that are known or reasonably knowable that, when considered in the aggregate, raise substantial doubt about the entity's ability to continue as a going concern within one year after the date that the consolidated financial statements are issued, for both annual and interim periods. ASU 2014-15 also requires certain disclosures around management's plans and evaluation, as well as the plans, if any, that are intended to mitigate those conditions or events that will alleviate the substantial doubt. ASU 2014-15 is effective for fiscal years ending after December 15, 2016. We adopted this guidance on July 5, 2016 (inception).

In March 2016, the FASB issued ASU No. 2016-09, Compensation—*Stock Compensation (Topic 718)*, or ASU 2016-09. The guidance changes how companies account for certain aspects of equity-based payments to employees. Entities will be required to recognize income tax effects of awards in the income statement when the awards vest or are settled. The guidance also allows an employer to repurchase more of an employee's shares than it can under current guidance for tax withholding purposes providing for withholding at the employee's maximum rate as opposed to the minimum rate without triggering liability accounting and to make a policy election to account for forfeitures as they occur. The updated guidance is effective for annual periods beginning after December 15, 2017. Early adoption is permitted. We adopted this guidance on July 5, 2016 (inception) and made the policy election to account for forfeitures as they occur. No awards have been forfeited as of December 31, 2017.

In November 2016, the FASB issued ASU 2016-18, *Statement of Cash Flows*, or ASU 2016-18, which requires that amounts generally described as restricted cash and restricted cash equivalents should be included with cash and cash equivalents when reconciling the beginning-of-period and end-of-period total amounts shown on the statement of cash flows. ASU 2016-18 is effective for fiscal years beginning after December 15, 2018 and should be applied using a retrospective transition method to each period presented. Early adoption is permitted. We do not expect the impact of ASU 2016-18 to be material to our consolidated financial statements.

In May 2017, the FASB issued ASU 2017-09, *Compensation—Stock Compensation* (Topic 718): Scope of Modification Accounting, or ASU 2017-09. ASC 2017-09 provides guidance about which changes to the terms or conditions of a share-based payment award require an entity to apply modification accounting in Topic 718. The guidance is effective for annual periods beginning after December 15, 2017, with early adoption permitted, including adoption in any interim period for which financial statements have not yet been issued. We are currently evaluating the potential effects of adopting the provisions of ASU 2017-09.

In July 2017, the FASB issued ASU 2017-11, *Accounting for Certain Financial Instruments with Down Round Features*, or ASU 2017-11, which updates the guidance related to the classification analysis of certain equity-linked financial instruments (or embedded features) with down round features. Under ASU 2017-11, a down round feature no longer precludes equity classification when assessing whether the instrument is indexed to an entity's own stock. As a result, a freestanding equity-linked financial instrument (or embedded conversion option) no longer would be accounted for as a derivative liability at fair value as a result of the existence of a down round feature. For freestanding equity classified financial instruments, the amendments require entities that present earnings per share (EPS) in accordance with Topic 260 to recognize the effect of the down round feature when it is triggered. That effect is treated as a dividend and as a reduction of income available to common shareholders in basic EPS. ASU 2017-11 is effective for public entities for all annual and interim periods beginning after December 15, 2019. Early adoption is permitted. We are currently evaluating the impact that the adoption of ASU 2017-11 will have on our consolidated financial statements.

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

We are exposed to market risk related to changes in interest rates. As of December 31, 2017, we had cash and cash equivalents of $53.3 million, primarily comprised of money market mutual funds consisting of U.S. government-backed securities. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments are in short-term securities. Our available for sale securities are subject to interest rate risk and will fall in value if market interest rates increase. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our portfolio.

We contract with CROs and contract manufacturers globally. We may be subject to fluctuations in foreign currency rates in connection with certain of these agreements. Transactions denominated in currencies other than the United States dollar are recorded based on exchange rates at the time such transactions arise. We have not engaged in the hedging of our foreign currency transactions to date, we are evaluating the costs and benefits of initiating such a program and may in the future hedge selected significant transactions denominated in currencies other than the U.S. dollar as we expand our international operation and our risk grows. As of December 31, 2017, substantially all of our total liabilities were denominated in the United States dollar.

Inflation generally affects us by increasing our cost of labor. We do not believe that inflation had a material effect on our business, financial condition or results of operations during the year ended December 31, 2017.

Item 8. Financial Statements and Supplementary Data.

Our consolidated financial statements, together with the report of our independent registered public accounting firm, appear on pages F-1 through F-23 of this Annual Report on Form 10-K.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure.

There has been no change of accountants nor any disagreements with accountants on any matter of accounting principles or practices or financial disclosure required to be reported under this Item.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

The Company has established disclosure controls and procedures designed to ensure that information required to be disclosed in the reports that the Company files or submits under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms and is accumulated and communicated to management, including the principal executive officer (our Chief Executive Officer) and principal financial officer (our Vice President, Finance), to allow timely decisions regarding required disclosure.

The Company's management, with the participation of the Company's Chief Executive Officer and Vice President, Finance, evaluated the effectiveness of the Company's disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of December 31, 2017. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Our disclosure controls and procedures have been designed to provide reasonable assurance of achieving their objectives. Based on the evaluation of the Company's disclosure controls and procedures as of December 31, 2017, the Company's Chief Executive Officer and Vice President, Finance concluded that, as of such date, the Company's disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control Over Financial Reporting

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

Changes in Internal Control over Financial Reporting

During the fiscal quarter ended December 31, 2017, we terminated our business services, personnel and information management agreement with PureTech Health, pursuant to which we shared administrative resources including legal, accounting and human resources support and computer systems. There was no other change in our internal control over financial reporting that occurred during the fiscal quarter ended December 31, 2017 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

Executive Officers and Directors

The following table sets forth the name, age as of March 23, 2018 and position of each of our executive officers and directors.

Name	Age	Position
Executive Officers		
Chen Schor(1)	45	President, Chief Executive Officer and Director
Joan Mannick, M.D.	59	Chief Medical Officer
John J. McCabe	50	Vice President, Finance
Non-Employee Directors		
Paul Fonteyne(2)(3)	56	Director
Jonathan Silverstein(2)(3)	51	Director
David Steinberg(1)(2)	45	Director
Lynne Sullivan(1)	52	Director
Daphne Zohar(3)	47	Director

(1) Member of audit committee
(2) Member of compensation committee
(3) Member of nominating and corporate governance committee

Executive Officers

Chen Schor has served as our President and Chief Executive Officer and as a member of our board of directors since our incorporation in July 2016. Mr. Schor previously served as President, Chief Executive Officer and director of Synta Pharmaceuticals Corp. from May 2015 until its merger with Madrigal Pharmaceuticals in July 2016, and prior to that, from 2014 until 2016, Mr. Schor served as its Executive Vice President and Chief Operation Officer. From 2012 to 2014, Mr. Schor served as President and Chief Executive Officer of Novalere FP, Inc., a pre-commercial stage allergy therapeutics company. From 2011 to 2012, Mr. Schor served as Chief Business Officer of Eleven Biotherapeutics, an emerging therapeutics company. From 2009 until 2011, Mr. Schor served as Vice President of Business Development, global branded products at Teva Pharmaceuticals. Prior to joining Teva, Mr. Schor was Chief Business Officer at Epix Pharmaceuticals, Inc. (formerly known as Predix Pharmaceuticals Inc.) from 2003 until 2009. Prior to joining Epix, Mr. Schor was a Partner at Yozma Venture Capital from 1998 until 2003, managing the fund's investments in biotechnology and medical device companies. Mr. Schor currently sits on the board of Brainstorm Cell Therapeutics Inc., a public biotechnology company. Mr. Schor received his MBA from Tel Aviv University, a B.A. in Economics and Accounting from Haifa University and a B.A. in Biology from Tel Aviv University. We believe that Mr. Schor is qualified to serve on our board of directors due to his service as our President and Chief Executive Officer and his extensive knowledge of our company and industry.

Joan Mannick, M.D., has served as our Chief Medical Officer since March 2017 and served as a member of our board of directors from March 2017 to November 2017. From November 2010 until March 2017, Dr. Mannick was Senior Director and subsequently Executive Director in the Translated Medical Division of NIBR, where Dr. Mannick led the clinical program at NIBR that targets pathways regulating aging to treat aging-related conditions. Prior to joining NIBR in 2010, Dr. Mannick was a Medical Director at Genzyme from 2007 to 2010 working in multiple therapeutic areas and a faculty member at Harvard Medical School from 1991 to 1999 and University of Massachusetts Medical School from 2000 to 2011. Her NIH-sponsored laboratory focused on the role of protein S-nitrosylation in physiology and pathophysiology. Dr. Mannick received her A.B. from Harvard College and her M.D. from Harvard Medical School. She completed her residency in Internal Medicine at Brigham and Women's Hospital and an Infectious Disease fellowship as part of the Harvard Combined Infectious Disease Program. We believe that Dr. Mannick is qualified to serve on our board of directors due to her industry and technical experience in the field in which we operate.

John J. McCabe, C.P.A., has served as our Vice President, Finance since October 2017. Mr. McCabe served as Chief Financial Officer for Eleven Biotherapeutics, Inc. from January 2016 until October 2017 and prior to that served as Senior Vice President from June 2013 to December 2015 and Director of Financial Reporting from April 2012 to June 2013. Mr. McCabe also provided independent financial and accounting consulting services from June 2011 to April 2012. Prior to that, Mr. McCabe served as Vice President of Finance at Clinical Data, Inc., from December 2010 to June 2011 and as the Senior Director of Financial Reporting of Clinical Data from August 2007 to December 2010. Prior to that, Mr. McCabe served in several financial roles at Interleukin Genetics, Inc. He began his career working for the accounting firm of Coopers & Lybrand LLP, now known as PricewaterhouseCoopers LLP. Mr. McCabe received a B.S. in Business Administration from the University of Vermont and is also a Certified Public Accountant.

Non-Employee Directors

Paul Fonteyne has served as a member of our board of directors since December 2017. Mr. Fonteyne has served as the United States Country Managing Director and President and Chief Executive Officer of Boehringer Ingelheim USA Corporation since 2011. Previously, Mr. Fonteyne served as Senior Corporate Vice President in Boehringer Ingelheim GmbH from 2009 to 2011. From 2003 to 2008 he served as Executive Vice President, Head of Marketing and Sales for Prescription Medicines at Boehringer-Ingelheim Pharmaceuticals, Inc. Prior to 2003, Mr. Fonteyne served in numerous leadership positions at Merck and Co. Inc, including Vice President of Sales in North Central US, Vice President of Marketing and Senior Director of Marketing. Mr. Fonteyne currently serves on an advisory board of Brigham and Woman's Hospital Lung Cancer Center and the board of PhRMA (the leading pharmaceutical association). Mr. Fonteyne received his MBA from Carnegie-Mellon University and his MS in Chemical Engineering from the Polytechnic School at the University of Brussels. We believe that Mr. Fonteyne is qualified to serve on our board of directors as a result of his past experience in the life science industry.

Jonathan Silverstein has served as a member of our board of directors since November 2017. Mr. Silverstein is currently a general partner at OrbiMed, a healthcare investment firm, where he has worked since December 1998. Previously, Mr. Silverstein was a director of life sciences in the investment banking department at Sumitomo Bank. Mr. Silverstein serves on the board of directors of Glaukos Corporation and Ascendis Pharma A/S. Mr. Silverstein also serves on the boards of directors of several private companies. Mr. Silverstein holds a B.A. from Denison University and a J.D. and M.B.A. from the University of San Diego. We believe that Mr. Silverstein's strategic development and capital markets experience qualifies him to serve on our board of directors.

David Steinberg has served as a member of our board of directors since March 2017. Mr. Steinberg is a Co-founder of PureTech Health plc and has been the Chief Innovation Officer for over five years. PureTech Health (PRTC.L) is an advanced clinical stage biopharma company developing new categories of medicines targeting the brain-immune-gut "BIG" axis. As a senior executive officer of PureTech Health, Mr. Steinberg is a member of the executive committee. He has been involved in initiating and leading multiple PureTech programs, including PureTech's microbiome initiative, lymphatic biology platform and immune-oncology pipeline. Prior to joining PureTech Health, he was a strategy consultant with Vertex Partners and the Boston Consulting Group, where he focused on research and development and product strategy and strategic alliances for Fortune 500 pharmaceutical and biotechnology clients. Mr. Steinberg is also a member of the UChicago Tech Innovation Fund Advisory Committee. He received his B.A. in Biology with distinction from Cornell University and graduated with high honors from the University of Chicago Booth School of Business with an M.B.A. in Strategy and Finance. We believe that Mr. Steinberg is qualified to serve on our board of directors due to his finance background and industry experience.

Lynne Sullivan has served as a member of our board of directors since December 2017. Ms. Sullivan is currently the Senior Vice President of Finance for Biogen, Inc., where she has worked since 2008. Ms. Sullivan has global responsibility for Biogen's Financial Planning & Analysis, Corporate Tax, and Corporate Finance groups, which includes ownership of long-range planning, capital allocation projects and the financial aspects of Mergers & Acquisitions/Business Development. Previously, Ms. Sullivan was the Vice President of Tax for Biogen, Vice President Tax for EMD Serono and the Vice President of Tax North America at Merck KgaA. She was also a Tax Partner at Arthur Anderson, where she led the North East Region's Tax Consulting Practice for the firm. Ms. Sullivan is on the Board of Solid Biosciences LLC, where she chairs the Audit Committee since 2015. Ms. Sullivan holds a B.S. in Accounting from Suffolk University and a M.S. in Taxation from Bentley College. We believe that Ms. Sullivan is qualified to serve on our board of directors due to her finance background and experience in the life sciences industry.

Daphne Zohar has served as a member of our board of directors since December 2017. Ms. Zohar is the founder and Chief Executive Officer of PureTech Health plc (PRTC.L), an advanced clinical stage biopharma company developing new categories of medicines targeting the brain-immune-gut "BIG" axis. Ms. Zohar has also co-founded and currently sits on the board of directors of a number of private life science companies, as well as on the board of PureTech Health plc, which is FTSE indexed and listed on the main market of the London Stock Exchange. Ms. Zohar also serves on the advisory board of the Technology Development Fund Advisory Board at Children's Hospital Boston, is an Editorial Advisor to Xconomy, a national news company, and is on the board of advisors of Life Science Cares. Ms. Zohar has been recognized as a leader and innovator in biotechnology by a number of sources, including Ernst & Young, BioWorld, MIT's Technology Review, the Boston Globe, and Scientific American. Ms. Zohar has been an entrepreneur since an early age and received her B.A. in entrepreneurship and new venture creation from Northeastern University. We believe that Ms. Zohar is qualified to serve on our board of directors given her experience and knowledge of the life science industry.

Section 16(a) Beneficial Ownership Reporting Compliance

Section 16(a) of the Exchange Act requires our directors, executive officers and beneficial owners of more than 10% of our equity securities to file reports of holdings and transactions in securities of the Company with the SEC. Our directors, executive officers and beneficial owners of more than 10% of our equity securities did not become subject to such Section 16(a) reporting requirements until January 25, 2018, after the completion of our fiscal year ended December 31, 2017.

Code of Business Conduct and Ethics

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. We have posted a copy of the code on the Corporate Governance section of our website. If we make any substantive amendments to, or grant any waivers from, the code of business conduct and ethics for 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.

Audit Committee

The members of our audit committee are Chen Schor, David Steinberg and Lynne Sullivan, and Lynne Sullivan is the chair of the audit committee. Our board of directors has determined that Lynne Sullivan is an "audit committee financial expert" as defined in applicable SEC rules and that each of the members of our audit committee possesses the financial sophistication required by audit committee members under Nasdaq rules.

Item 11. Executive Compensation.

This section describes the material elements of compensation awarded to, earned by or paid to our named executive officers in 2017, who were Chen Schor, our President and Chief Executive Officer, Joan Mannick, our Chief Medical Officer, and John McCabe, our Vice President, Finance. These individuals represent our principal executive officer and our next two most highly compensated executive officers in the year ended December 31, 2017. We are an "emerging growth company," within the meaning of the JOBS Act, and have elected to comply with the reduced compensation disclosure requirements available to emerging growth companies under the JOBS Act. This section also provides qualitative information regarding the manner and context in which compensation is awarded to and earned by our named executive officers and is intended to place in perspective the data presented in the tables and narrative that follow.

2017 Summary Compensation Table

The following table sets forth information regarding compensation awarded to, earned by or paid to our named executive officers during 2017 and 2016.

Name and Principal Position	Year	Salary ($)	Option Awards ($)(1)	Non-Equity Incentive Compensation ($)(2)		All Other Compensation ($)(3)	Total ($)
Chen Schor(4)	2017	268,826	—	209,280	(5)	7,400	485,506
President and Chief Executive Officer	2016	—	—	—		—	—
Joan Mannick(6)	2017	236,035	—	163,665	(5)	6,484	406,184
Chief Medical Officer							
John McCabe(7)	2017	47,526	485,474	15,822	(5)	314	549,136
Vice President, Finance							

(1) The amounts reported in the "Option Awards" column reflects the aggregate grant date fair value of share- based compensation awarded during the year computed in accordance with the provisions of Financial Accounting Standards Board Accounting Standards Codification, or ASC, Topic 718. See Note 2 to our consolidated financial statements appearing at the end of this Annual Report on Form 10-K regarding assumptions underlying the valuation of equity awards.

(2) Each of our named executive officers is eligible to earn cash incentive compensation for 2017 based upon performance in 2017 and the achievement of clinical and developmental objectives.

(3) Amounts reflecting Company matching contributions to our 401(k) plan.

(4) Mr. Schor has served as a director and as our President and Chief Executive Officer since July 2016, but did not become an employee of our company until April 4, 2017. Mr. Schor did not earn any compensation for his services until he commenced his employment relationship with us in 2017. In 2016, he purchased 1,886,363 shares of restricted common stock as founder shares at the then-current fair market value.

(5) Amounts include annual performance-based bonuses earned by Mr. Schor, Dr. Mannick and Mr. McCabe of $173,280, $133,665 and $15,822, respectively, for 2017. In addition, the amount for Mr. Schor and Dr. Mannick represent bonuses of $36,000 and $30,000, respectively, paid upon achievement of certain milestones in 2017 as further described below.

(6) Dr. Mannick commenced her employment with us in April 2017.

(7) Mr. McCabe commenced his employment with us in October 2017.

Narrative to Summary Compensation Table

Our sole executive officer during 2016 was our President and Chief Executive Officer, Chen Schor. Mr. Schor did not receive any cash compensation for his services in 2016, but purchased restricted stock at the then-current fair market value at incorporation.

In March 2017, we appointed Dr. Joan Mannick as our Chief Medical Officer. In April 2017, Mr. Schor and Dr. Mannick commenced an employment relationship with us, and at that time, began receiving base salary and eligibility for performance-based bonuses, as described in greater detail below under "—Employment Arrangements with Our Named Executive Officers." John McCabe, our Vice President, Finance, has provided consulting services to us since September 2017, and was appointed to his current position in October 2017.

In July 2016, the board of directors issued and sold at the then-current fair market value 1,886,363 shares of restricted common stock to each of Mr. Schor and Dr. Mannick as founder shares. These equity awards are subject to a repurchase option in favor of us, pursuant to which we may repurchase any unvested shares at the purchase price paid for such shares in the event that either Mr. Schor or Dr. Mannick ceases providing services to us. In the case of a qualified funding (as defined in the applicable award agreement), which was satisfied upon the closing of our Series A preferred stock financing, a portion of the unvested shares accelerated and vested in full. In the case of a liquidity event (as defined in the applicable award agreement), which includes our initial public offering, the remaining unvested shares will accelerate and vest in full.

We use base salaries and performance-based bonuses to recognize the experience, skills, knowledge and responsibilities required of all our employees, including our named executive officers. Although we do not have a formal

policy with respect to the grant of equity incentive awards to our current and future named executive officers, we believe that equity grants provide these officers with a strong link to our long-term performance, create an ownership culture and help to align the interests of these officers and our stockholders. In addition, we believe that equity grants with a time-based vesting feature promote executive retention because this feature incents our current and future named executive officers to remain in our employment during the vesting period. Accordingly, our board of directors intends to periodically review the equity incentive compensation of our current and future named executive officers and from time to time may grant equity incentive awards to them in the form of stock options.

Annual performance-based bonuses, which are paid in cash, were included as a component of the executive compensation to motivate our executive officers to achieve key corporate, financial and strategic goals. The amounts approved and paid to Mr. Schor, Dr Mannick and Mr. McCabe were $173,280, $133,665 and $15,822, respectively, for 2017 and were included in the "Non-Equity Incentive Compensation" column of the summary compensation table above.

Beginning with annual bonuses for fiscal year 2018, our board of directors has adopted the Senior Executive Cash Incentive Bonus Plan, or the Bonus Plan. The Bonus Plan provides for cash bonus payments based upon the attainment of performance targets established by our compensation committee. The payment targets will be related to financial and operational measures or objectives with respect to our company, or corporate performance goals, as well as individual performance objectives.

Our compensation committee may select corporate performance goals from among the following: cash flow (including, but not limited to, operating cash flow and free cash flow); research and development, publication, clinical and/or regulatory milestones; earnings before interest, taxes, depreciation and amortization; net income (loss) (either before or after interest, taxes, depreciation and/or amortization); changes in the market price of the Company’s common stock; economic value-added; acquisitions or strategic transactions, including licenses, collaborations, joint ventures or promotion arrangements; operating income (loss); return on capital, assets, equity, or investment; total stockholder returns; coverage decisions; productivity; expense efficiency; margins; operating efficiency; working capital; earnings (loss) per share of the Company’s common stock; sales or market shares; number of prescriptions or prescribing physicians; revenue; corporate revenue; operating income and/or net annual recurring revenue, any of which may be measured in absolute terms, as compared to any incremental increase, in terms of growth, or as compared to results of a peer group.

Each executive officer who is selected to participate in the Bonus Plan will have a target bonus opportunity set for each performance period. The bonus formulas will be adopted in each performance period by the compensation committee and communicated to each executive. The corporate performance goals will be measured at the end of each performance period after our financial reports have been published or such other appropriate time as the compensation committee determines. If the corporate performance goals and individual performance objectives are met, payments will be made as soon as practicable following the end of each performance period. Subject to the rights contained in any agreement between the executive officer and us, an executive officer must be employed by us on the bonus payment date to be eligible to receive a bonus payment. The Bonus Plan also permits the compensation committee to approve additional bonuses to executive officers in its sole discretion and provides the compensation committee with discretion to adjust the size of the award as it deems appropriate to account for unforeseen factors beyond management’s control that affected corporate performance.

Outstanding Equity Awards at 2017 Year End

The following table sets forth information regarding outstanding equity awards held by our named executive officers as of December 31, 2017:

	Option Awards				Stock Awards Number	
Name	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price ($)	Option Expiration Date	Number of Shares of Stock that have not Vested (#)	Market Value of Shares of Stock that have not Vested ($)
Chen Schor	—	—	—	—	548,224 (1)	7,220,110
Joan Mannick	—	—	—	—	548,224 (1)	7,220,110
John McCabe	—	78,100 (2)	9.33	12/4/2027	—	—

(1) These shares of restricted stock were issued on July 11, 2016 to Mr. Schor and Dr. Mannick, and vest in 48 equal monthly installments through July 11, 2020. Upon the closing of a liquidity event (as defined in the award agreement), which includes our initial public offering, the unvested shares of restricted stock will accelerate and vest in full.

(2) On December 5, 2017, Mr. McCabe was awarded an option to purchase 78,100 shares of our common stock under our 2017 Plan. The shares underlying this option vest as follows: 25% of the shares vest on October 23, 2018, and the remaining shares vest in six equal semi-annual installments following October 23, 2018, subject to Mr. McCabe's continued service.

Employment Arrangements with Our Named Executive Officers

In connection with their commencement of employment with us, we have entered into employment offer letters with each of our named executive officers. Mr. Schor's and Dr. Mannick's offer letters have been amended upon the closing of our IPO.

Chen Schor Offer Letter

In March 2017, we entered into an offer letter with Mr. Schor. The offer letter established Mr. Schor's title, his base salary of $361,000 per year, his eligibility for an annual bonus and certain milestone-based bonuses, and his eligibility for benefits made available to employees generally and also provides for certain benefits upon termination of his employment under specified conditions. Our board of directors determined that Mr. Schor was eligible to receive an annual bonus of up to 40% of his base salary, including a bonus at the same rate for the period from January 1, 2017 through March 31, 2017, when his offer letter was signed.

Mr. Schor's offer letter also provided for the following milestone-based bonuses. Mr. Schor will receive a bonus of: (i) $18,000 after the first subject is dosed in a Phase 2 study following the pre-IND meeting or call with the FDA (or written feedback to a pre-IND briefing book from the FDA) provided such dosing occurs by April 4, 2018; (ii) $18,000 after we enroll the first subject following interim analysis review by a committee defined by the Phase 2 study protocol, provided such enrollment occurs by April 4, 2019; and (iii) $36,000 after we achieve the primary end point with a p-value equal to or less than 0.05 in a Phase 2 study, provided such achievement occurs by April 4, 2020. In the event that Mr. Schor earns the bonus described in clause (iii) of the prior sentence but has not yet earned the bonuses described in clauses (i) and (ii), such bonuses will be payable at that time.

Mr. Schor's employment is at will. Under the terms of his offer letter, if Mr. Schor's employment is terminated by us without cause or by Mr. Schor for good reason, each as defined in his offer letter, and subject to Mr. Schor's execution of a general release of potential claims against us, we have agreed to pay Mr. Schor an amount equal to 6 months of his then-current base salary and provide continued coverage under our health and dental plans for 6 months if such termination occurs within the first 12 months of his employment or an amount equal to 12 months of his then-current base salary and continued coverage under our health and dental plans for 12 months if such termination occurs thereafter. In addition, if such termination occurs following a change in control, Mr. Schor will also be eligible to receive a pro-rated portion of his annual performance bonus for the calendar year in which his employment was terminated.

Mr. Schor's offer letter also provides that he will (1) not compete with us during his employment and for a period of six months after the termination of his employment, (2) not solicit our employees, independent contractors or customers during his employment and for a period of six months after the termination of his employment, (3) protect our confidential and proprietary information and (4) assign to us related intellectual property developed during the course of his employment.

We amended Mr. Schor's offer letter, effective upon the closing of our IPO. Pursuant to this amendment, Mr. Schor will be entitled to receive an annual base salary of $450,000 and an annual target bonus equal to 50% of his annual base salary. Mr. Schor's amended offer letter provides that, in the event that his employment is terminated by us without cause or by him for good reason, and such termination occurs within the 12-month period following a change of control, then in lieu of the payments and benefits described above, Mr. Schor shall be entitled to receive (i) a lump sum cash payment equal to 1.5 times the sum of his base salary and target annual incentive compensation, (ii) continued coverage under our health and dental plans for up to 18 months following termination and (iii) full acceleration of all time-based stock options and other time-based stock-based awards held by Mr. Schor.

In connection with our IPO, we granted to Mr. Schor a stock option to purchase 238,311 shares of our common stock, at an exercise of $15.00 per share. Such option will vest 25% on the first anniversary of the grant date, and the remainder ratably each month over the remaining three years.

Joan Mannick Offer Letter

In March 2017, we entered into an offer letter with Dr. Mannick. The offer letter established Dr. Mannick's title, her base salary of $318,250 per year, her eligibility for an annual bonus and certain milestone-based bonuses, and her eligibility for benefits made available to employees generally and also provides for certain benefits upon termination of her employment under specified conditions. Dr. Mannick's annual base salary shall be subject to increase in the discretion of our board of directors; provided that her base salary shall be increased by no less than 5% upon the earlier of April 4, 2019 or her eligibility to receive the bonus described in clause (iii) of the following paragraph. Our board of directors determined that Dr. Mannick is eligible to receive an annual bonus of up to 35% of her base salary, and a bonus at the rate of 23.33% for the period from January 1, 2017 through March 31, 2017, when her offer letter was signed.

Dr. Mannick's offer letter also provided for the following milestone-based bonuses. Dr. Mannick will receive a bonus of: (i) $15,000 after the first subject is dosed in a Phase 2 study following the pre-IND meeting or call with the FDA (or written feedback to a pre-IND briefing book from the FDA) provided such dosing occurs by April 4, 2018; (ii) $15,000 after we enroll the first subject following interim analysis review by a committee defined by the Phase 2 study protocol, provided such enrollment occurs by April 4, 2019; and (iii) $30,000 after we achieve the primary end point with a p-value equal to or less than 0.05 in a Phase 2 study, provided such achievement occurs by April 4, 2020. In the event that Dr. Mannick earns the bonus described in clause (iii) of the prior sentence but has not yet earned the bonuses described in clauses (i) and (ii), such bonuses will be payable at that time.

Dr. Mannick's employment is at will. Under the terms of her offer letter, if Dr. Mannick's employment is terminated by us without cause or by Dr. Mannick for good reason, each as defined in her offer letter, and subject to Dr. Mannick's execution of a general release of potential claims against us, we have agreed to pay

Dr. Mannick an amount equal to 6 months of her then-current base salary and provide continued coverage under our health and dental plans for 6 months if such termination occurs within the first 12 months of her employment or an amount equal to 9 months of her then-current base salary and continued coverage under our health and dental plans for 9 months if such termination occurs thereafter. In addition, if such termination occurs following a change in control, Dr. Mannick will also be eligible to receive a pro-rated portion of her annual performance bonus for the calendar year in which her employment was terminated.

Dr. Mannick's offer letter also provides that she will (1) not compete with us during her employment and for a period of six months after the termination of her employment, (2) not solicit our employees, independent contractors or customers during her employment and for a period of six months after the termination of her employment, (3) protect our confidential and proprietary information and (4) assign to us related intellectual property developed during the course of her employment.

We amended Dr. Mannick's offer letter, effective upon the closing of our IPO. Pursuant to this amendment, Dr. Mannick's base salary will be increased to $360,000 per year. Dr. Mannick's amended offer letter provides that, in the event that her employment is terminated by us without cause or by her for good reason, and such termination occurs within the 12-month period following a change of control, then in lieu of the payments and benefits described above, Dr. Mannick shall be entitled to receive (i) a lump sum cash payment equal to the sum of her base salary and target annual incentive compensation, (ii) continued coverage under our health and dental plans for up to 12 months following termination and (iii) full acceleration of all time-based stock options and other time-based stock-based awards held by Dr. Mannick.

In connection with our IPO, we granted to Dr. Mannick a stock option to purchase 92,999 shares of our common stock, at an exercise price equal of $15.00 per share. Such option will vest 25% on the first anniversary of the grant date, and the remainder ratably each month over the remaining three years.

In addition, we have entered into a letter agreement with Dr. Mannick, effective from and after the closing of our IPO, to provide her with certain rights to participate in meetings of our board of directors as a non-voting observer and to receive copies of materials provided to our board of directors. We may exclude Dr. Mannick from such participation for any reason, including if we believe that such exclusion is reasonably necessary to preserve the attorney-client privilege, to protect confidential proprietary information or for other similar reasons. The observer rights will terminate in the event that Dr.

Mannick is no longer serving as an officer of our company for any reason, or if she materially breaches any employment agreement or confidentiality agreement with us, or if we undergo a merger or consolidation.

John McCabe

In October 2017, we entered into an offer letter with Mr. McCabe. The offer letter established Mr. McCabe's title, his base salary of $250,000 per year, his eligibility for an annual bonus, and his eligibility for benefits made available to employees generally and also provides for certain benefits upon termination of his employment under specified conditions. Our board of directors determined that Mr. McCabe is eligible to receive an annual bonus of up to 30% of his base salary, pro-rated for 2017 to reflect his partial year of employment.

Mr. McCabe's employment is at will. Under the terms of his offer letter, if Mr. McCabe's employment is terminated by us without cause or by Mr. McCabe for good reason, each as defined in his offer letter, and such termination occurs following the 12-month anniversary of his start and not in connection with a change in control, then subject to Mr. McCabe's execution of a general release of potential claims against us and continued compliance with the restrictive covenants described below, we have agreed to pay Mr. McCabe an amount equal to three months of his then-current base salary and provide continued coverage under our health and dental plans on the same terms and conditions in effect prior to his termination until the earlier of the expiration of the three- month period for which he is entitled to receive severance and the date Mr. McCabe commences new employment which offers health coverage. If Mr. McCabe's employment is terminated by us without cause or by Mr. McCabe for good reason within 12 months after a change in control, and subject to Mr. McCabe's execution of a general release of potential claims against us and continued compliance with the restrictive covenants described below, we have agreed to pay Mr. McCabe (1) an amount equal to six months of his then-current base salary, (2) up to 50% of a pro-rated portion of his annual performance bonus for any partial year of service and (3) continued coverage under the Company's health and dental plans until the earlier of the expiration of 6 months and the date Mr. McCabe commences new employment which offers health coverage. In addition, all equity-based awards held by Mr. McCabe shall accelerate in full.

Mr. McCabe's offer letter also provides that he will (1) not compete with us during his employment and for a period of one year after the termination of his employment, (2) not solicit our employees, independent contractors or customers during his employment and for a period of one year after the termination of his employment, (3) protect our confidential and proprietary information and (4) assign to us related intellectual property developed during the course of his employment.

401(k) Retirement Plan

We participate in a 401(k) retirement plan sponsored by PureTech Health, our shareholder, that is intended to be a tax-qualified defined contribution plan under Section 401(k) of the Internal Revenue Code. In general, all of our employees are eligible to participate, beginning two months after the commencement of their employment. The 401(k) plan includes a salary deferral arrangement pursuant to which participants may elect to reduce their current compensation by up to the statutorily prescribed limit and have the amount of the reduction contributed to the 401(k) plan. We currently contribute to each employee's 401(k) account, in the first quarter of each year, 3% of his or her eligible earnings from the prior year.

Hedging and Pledging Prohibitions

Our insider trading policy expressly prohibits short sales and derivative transactions of our stock by our named executive officers, directors and specified other employees, including short sales of our securities, including short sales "against the box." Our insider trading policy expressly prohibits, without the advance approval of our audit committee, purchases or sales of puts, calls or other derivative securities of the company or any derivative securities that provide the economic equivalent of or monetization transactions accomplished through the use of prepaid variable forwards, equity swaps, collars and exchange funds.

Limitations on Liability and Indemnification

As permitted by Delaware law, our board of directors and stockholders adopted provisions in our certificate of incorporation, which become effective as of the closing date of our IPO, that limit or eliminate the personal liability of our directors. Our certificate of incorporation limits the personal liability of directors for breach of fiduciary duty to the maximum extent permitted by the General Corporation Law of the State of Delaware and provides that no director will have

personal liability to us or to our stockholders for monetary damages for breach of fiduciary duty. However, these provisions do not eliminate or limit the liability of any of our directors:

- for any breach of the director's duty of loyalty to us or our stockholders;
- for acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;
- for voting for or assenting to unlawful payments of dividends, stock repurchases or other distributions; or
- for any transaction from which the director derived an improper personal benefit.

Any amendment to or repeal of these provisions will not eliminate or reduce the effect of these provisions in respect of any act, omission or claim that occurred or arose prior to such amendment or repeal. If the General Corporation Law of the State of Delaware is amended to provide for further limitations on the personal liability of directors of corporations, then the personal liability of our directors will be further limited to the greatest extent permitted by the General Corporation Law of the State of Delaware.

In addition, our certificate of incorporation provides that we must indemnify our directors and officers and we must advance expenses, including attorneys' fees, to our directors and officers in connection with legal proceedings, subject to very limited exceptions.

We maintain a general liability insurance policy that covers specified liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers. In addition, we entered into indemnification agreements with each of our officers and directors prior to the completion of our IPO. These indemnification agreements will require us, among other things, to indemnify each such director or officer for some expenses, including attorneys' fees, judgments, fines and settlement amounts, incurred by him or her in any action or proceeding arising out of his or her service as one of our directors or officers.

Some of our non-employee directors may, through their relationships with their employers, be insured or indemnified against specified liabilities incurred in their capacities as members of our board of directors.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, executive officers or persons controlling us, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

Rule 10b5-1 Sales Plans

Our directors and executive officers may adopt written plans, known as Rule 10b5-1 plans, in which they will contract with a broker to buy or sell shares of our common stock on a periodic basis. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the director or officer when entering into the plan, without further direction from the director or officer. The director or officer may amend or terminate the plan in some circumstances. Our directors and executive officers may also buy or sell additional shares outside of a Rule 10b5-1 plan when they are not in possession of material, nonpublic information.

Compensation Risk Assessment

We believe that although a portion of the compensation provided to our executive officers and other employees is performance-based, our executive compensation program does not encourage excessive or unnecessary risk taking. This is primarily due to the fact that our compensation programs are designed to encourage our executive officers and other employees to remain focused on both short-term and long-term strategic goals, in particular in connection with our pay-for-performance compensation philosophy. As a result, we do not believe that our compensation programs are reasonably likely to have a material adverse effect on us.

Director Compensation

We have historically not compensated our directors for their services to us. We reimburse our non-employee directors for reasonable travel and out-of-pocket expenses incurred in connection with attending board of directors and committee meetings.

Non-Employee Director Compensation Policy

Our board of directors has approved a compensation policy, effective as of the completion of our IPO, which is designed to enable us to attract and retain qualified and experienced individuals to serve as directors and to align our directors' interests with those of our stockholders.

Under the policy, each director who is not an employee will be paid cash compensation from and after the completion of our IPO, as set forth below:

	Member Annual Fee	Chairperson Additional Annual Fee
Board of Directors	$ 35,000	$ 30,000
Audit Committee	7,500	7,500
Compensation Committee	5,000	5,000
Nominating and Corporate Governance Committee	4,000	4,000

Each annual cash retainer will be payable in arrears in four quarterly installments on the last day of each quarter, provided that the amount of each payment will be prorated for any portion of a quarter that a director is not serving on our board of directors.

In addition, each new non-employee director elected to our board of directors will be granted an initial, one-time equity award of options to purchase 28,828 shares of our common stock on the date of such director's election or appointment to the board of directors, which will vest in the following manner, subject to continued service through such vesting date: 33% on first anniversary of grant, then the remainder should vest ratably monthly over two years. On the date of each annual meeting of stockholders of our company, each non-employee director will be granted an option to purchase 14,414 shares of our common stock, which will vest in the following manner, subject to continued service as a director through such vesting date: in full upon the earlier to occur of the first anniversary of the date of grant or the date of the next annual meeting.

Compensation Committee Interlocks and Insider Participation

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

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

Securities Authorized for Issuance under Equity Compensation Plans

The following table shows information relating to our equity compensation plan as of December 31, 2017. As of December 31, 2017, we had one equity compensation plan, our 2017 Plan, which was approved by our board of directors and our stockholders.

	Equity Compensation Plan Information		
Plan Category	Number of securities to be issued upon exercise of outstanding options, warrants and rights	Weighted average exercise price of outstanding options, warrants and rights	Number of securities remaining available for future issuance under equity compensation plans (excluding securities in first column)
Equity compensation plans approved by security holders	195,668	$ 4.49	1,670,341
Equity compensation plans not approved by security holders	—	—	—
Total	195,668	$ 4.49	1,670,341

As described above under “Item 11. Executive Compensation”, in connection with our IPO, our board of directors and stockholders approved two new equity compensation plans, the 2018 Plan and the ESPP. The 2018 Plan and ESPP became effective on January 24, 2018. The table above does not include any amounts issuable under either the 2018 Plan or the ESPP.

Security Ownership of Certain Beneficial Owners and Management

The following table sets forth information with respect to the beneficial ownership of our common stock as of March 23, 2018 by:

- each of our directors;
- our named executive officer;
- all of our directors and executive officers as a group; and
- each person, or group of affiliated persons, who is known by us to beneficially own more than 5% of our common stock.

The column entitled “Percentage of Shares Beneficially Owned” is based on a total of 28,046,315 shares of our common stock outstanding as of March 23, 2018.

Beneficial ownership is determined in accordance with the rules and regulations of the SEC and includes voting or investment power with respect to our common stock. Shares of our common stock subject to options that are currently exercisable or exercisable within 60 days after March 23, 2018 are considered outstanding and beneficially owned by the person holding the options for the purpose of calculating the percentage ownership of that person but not for the purpose of calculating the percentage ownership of any other person. Except as otherwise noted, the persons and entities in this table have sole voting and investment power with respect to all of the shares of our common stock beneficially owned by them, subject to community property laws, where applicable. Except as otherwise set forth below, the address of the beneficial owner is c/o resTORbio, Inc., 500 Boylston Street, 12th Floor, Boston, Massachusetts 02116.

Name of Beneficial Owner	Shares Beneficially Owned	Percentage of Shares Beneficially Owned
5% Stockholders		
PureTech Health LLC(1)	9,800,396	34.9%
Novartis Institutes for BioMedical Research, Inc.(2)	2,021,237	7.2%
OrbiMed Private Investments VI, LP(3)	4,830,387	17.2%
FMR LLC(4)	3,038,509	10.8%
Named Executive Officer, Other Executive Officers and Directors		
Chen Schor	1,886,363	6.7%
Paul Fonteyne	—	*%
Joan Mannick, M.D.	1,886,363	6.7%
John McCabe	—	*%
Jonathan Silverstein	—	*%
David Steinberg	—	*%
Lynne Sullivan	—	*%
Daphne Zohar	—	*%
All Current Executive Officers and Directors as a Group (8 persons)	3,772,726	17.5%

* Represents beneficial ownership of less than 1% of our outstanding stock.

(1) Voting and investment power over the shares held by PureTech Health LLC is exercised by its parent entity, PureTech Health plc. The board of directors of PureTech Health plc consists of Mr. Joi Ito, Dr. Raju Kucherlapati, Dr. John LaMattina, Dr. Robert Langer, Dame Marjorie Scardino, Dr. Ben Shapiro, Mr. Christopher Viehbacher, Ms. Daphne Zohar and Mr. Stephen Muniz. None of the members of the board of directors of PureTech Heath plc or PureTech Health LLC has individual voting or investment power with respect to such shares. The address for PureTech Health LLC and the individuals listed above is c/o PureTech Health LLC, 501 Boylston Street, Suite 6102, Boston, MA 02116.

(2) All shares are held by NIBR. NIBR is an indirect wholly-owned subsidiary of, and controlled by, Novartis AG. The address for NIBR is 250 Massachusetts Avenue, Cambridge, MA 02139.

(3) All shares are held by OrbiMed Private Investments VI, LP (“OPI VI”). OrbiMed Capital GP VI LLC (“GP VI”) is the sole general partner of OPI VI. OrbiMed Advisors LLC (“OrbiMed Advisors”) is the managing member of GP VI. Samuel D. Isaly is the managing member of and owner of a controlling interest in OrbiMed Advisors. By virtue of such relationships, GP VI, OrbiMed Advisors, and Mr. Isaly may be deemed to have voting and investment power with respect to the shares held by OPI VI and as a result may be deemed to have beneficial ownership of such shares. Jonathan T. Silverstein, a member of OrbiMed Advisors, is a member of our board of directors. Each of GP VI, OrbiMed Advisors, Mr. Isaly and Mr. Silverstein disclaims beneficial ownership of the shares held by OPI VI, except to the extent of its or his pecuniary interest therein if any. The address of these entities is 601 Lexington Avenue, 54th floor, New York, New York 10022.

(4) Information herein is based on a Schedule 13G filed by FMR LLC with the SEC on March 12, 2018. FMR LLC, a parent holding company, has sole voting power over 255,897 shares and sole dispositive power over 3,038,509 shares. Abigail P. Johnson is a Director, Chairman and Chief Executive Officer of FMR LLC. Members of the Johnson family, including Abigail P. Johnson, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR LLC, representing 49% of the voting power of FMR LLC. The Johnson family group and all other Series B shareholders have entered into a shareholders' voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of voting common shares and the execution of the shareholders' voting agreement, members of the Johnson family may

be deemed, under the Investment Company Act of 1940, to form a controlling group with respect to FMR LLC. Neither FMR LLC nor Abigail P. Johnson has the sole power to vote or direct the voting of the shares owned directly by the various investment companies registered under the Investment Company Act, or Fidelity Funds, advised by Fidelity Management & Research Company, or FMR Co, a wholly owned subsidiary of FMR LLC, which power resides with the Fidelity Funds' Boards of Trustees. FMR Co carries out the voting of the shares under written guidelines established by the Fidelity Funds' Boards of Trustees. The address for FMR LLC is 82 Devonshire Street, Boston, Massachusetts 02109.

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

Other than the compensation agreements and other arrangements described under “Executive Compensation,” “Director Compensation” and “Non-Employee Director Compensation” in this Annual Report on Form 10-K and the transactions described below, since January 1, 2017, there has not been and there is not currently proposed, any transaction or series of similar transactions to which we were, or will be, a party in which the amount involved exceeded $120,000 and in which any of our directors, executive officers or beneficial holders of more than 5% of any class of our voting securities, or any member of the immediate family of, or entities affiliated with, any of the foregoing persons, had, or will have, a direct or indirect material interest.

Founders Shares

On March 1, 2017, we issued 1,886,363 shares of our common stock to PureTech Health as founder shares at par value, the fair market value of the shares at the time of their issuance for an aggregate price of $242.

Series A Preferred Stock Financing

In March 2017, we entered into a Series A preferred stock purchase agreement for the sale of up to 10,351,968 shares of Series A preferred stock in one or more closings at a price per share of $1.932. In March 2017, we issued and sold an aggregate of 5,434,783 shares of our Series A preferred stock in the first closing of our Series A preferred stock financing. PureTech Health paid $5,017,989 for such Series A shares, and the remaining $482,011 of the purchase price was net settled against invoices paid by PureTech Health on our behalf prior to the closing of our Series A financing and as reimbursement for certain due diligence costs incurred in connection with the financing. The shares of Series A preferred stock issued to NIBR were issued in consideration for a license from Novartis, as discussed further below. The Series A preferred stock purchase agreement provided that, after the initial closing, PureTech Health would purchase up to an additional 4,917,185 shares of Series A preferred stock at $1.932 per share at future dates based on the occurrence of certain events as specified under the agreement. In addition, we entered into a side letter with PureTech Health under which PureTech Health agreed to purchase up to 5,175,984 additional shares of Series A preferred stock at $1.932 per share at a future date based on the occurrence of certain events as specified under the letter. We refer to these agreements to purchase such additional shares as the tranche rights. Such tranche rights were exercised to the extent described below, and, as of the date of this Annual Report on Form 10-K, have been terminated.

The following table sets forth the number of shares of our Series A preferred stock purchased by our directors, executive officers and 5% stockholders and their affiliates and the aggregate purchase price paid for such shares. Upon the closing of our IPO, each share of preferred stock automatically converted into shares of common stock on a 1.2804-to-1 ratio.

Name	Shares of Series A Preferred Stock Purchased	Aggregate Cash Purchase Price
PureTech Health LLC	2,846,791	$ 5,500,001
Novartis Institutes for Biomedical Research, Inc.	2,587,992	—
Total	5,434,783	$ 5,500,001

In August 2017, we issued and sold an additional 2,329,193 shares of our Series A preferred stock at a price per share of $1.932 in the second closing of our Series A preferred stock financing, for a purchase price of approximately $4.5 million. The following table sets forth the number of shares of our Series A preferred stock purchased by our directors, executive officers and 5% stockholders and their affiliates and the aggregate purchase price paid for such shares. Upon the closing of our IPO, each share of preferred stock automatically converted into shares of common stock on a 1.2804-to-1 ratio.

Name	Shares of Series A Preferred Stock Purchased	Aggregate Purchase Price
PureTech Health LLC	2,329,193	$ 4,500,001
Total	2,329,193	$ 4,500,001

In October 2017, we issued and sold an additional 7,763,975 shares of our Series A preferred stock at a price per share of $1.932 in the third and final closing of our Series A preferred stock financing, for a purchase price of approximately $15.0 million. The following table sets forth the number of shares of our Series A preferred stock purchased by our directors, executive officers and 5% stockholders and their affiliates and the aggregate purchase price paid for such shares. Upon the closing of our IPO, each share of preferred stock automatically converted into shares of common stock on a 1.2804-to-1 ratio.

Name	Shares of Series A Preferred Stock Purchased	Aggregate Cash Purchase Price
PureTech Health LLC	4,658,385	$ 9,000,000
OrbiMed Private Investments VI, LP	3,105,590	6,000,000
Total	7,763,975	$ 15,000,000

Series B Preferred Stock Financing

In October 2017, we entered into a Series B preferred stock purchase agreement for the sale of up to 4,792,716 shares of Series B preferred stock in one or more closings at a price per share of $8.346. In November 2017, we issued and sold an aggregate of 4,792,716 shares of our Series B preferred stock for gross proceeds of approximately $40.0 million. The following table sets forth the number of shares of our Series B preferred stock purchased by our directors, executive officers and 5% stockholders and their affiliates and the aggregate purchase price paid for such shares. Upon the closing of our IPO, each share of preferred stock automatically converted into shares of common stock on a 1.2804-to-1 ratio.

Name	Shares of Series B Preferred Stock Purchased	Aggregate Cash Purchase Price
OrbiMed Private Investments VI, LP	2,396,358	$ 20,000,004
Total	2,396,358	$ 20,000,004

Participation in our Initial Public Offering

Our existing stockholders, including certain affiliates of our directors, purchased shares of our common stock in our IPO at the initial public offering price. The following table sets forth the number of shares our common stock purchased directors, executive officers and 5% stockholders and their affiliates and the aggregate purchase price paid for such shares.

Name	Shares of Common Stock Purchased	Aggregate Cash Purchase Price
PureTech Health LLC	233,333	3,499,995
Orbimed Advisors LLC	533,333	7,999,995
Total	766,666	$ 11,499,990

License Agreement with Novartis

In March 2017, we entered into a license agreement with Novartis pursuant to which we were granted an exclusive worldwide license to certain intellectual property rights owned or controlled by Novartis, including patents, patent applications, proprietary information, know-how and other intellectual property, to develop, commercialize and sell one or more therapeutic products comprising RTB101 or RTB101 and everolimus in a fixed dose combination. See “Business—Intellectual Property—License Agreement with Novartis.”

PureTech Health Shared Resources

PureTech Health was a founder of our company and in that capacity had provided us with strategic medical, clinical and scientific advice pursuant to a business services, personnel and information management agreement. PureTech Health also played a significant role in securing our foundational intellectual property from Novartis, leveraging its connections to establish the relationship, assisting in the negotiation of the license agreement and providing strategic advice throughout the process. In addition, we shared administrative resources and offices with PureTech Health, including legal, accounting and human resources support, computer and telecommunications systems and other office infrastructure through December 31, 2017. Beginning in April 2017, PureTech has invoiced us at cost for such services, with such amounts totaling $202,306 as of December 31, 2017. In addition, PureTech Health periodically invoiced us for reimbursement of out of pocket expenses reasonably incurred on our behalf in connection with providing such business services.

Investors’ Rights Agreement

We are a party to an investors’ rights agreement, dated as of November 29, 2017, with holders of our preferred stock, including some of our 5% stockholders and entities affiliated with our directors. Such holders consisted of entities affiliated with OrbiMed, PureTech Health and Novartis, each a 5% stockholder. Each of PureTech Health and OrbiMed have appointed representatives to our board of directors. The investor rights agreement provides these holders the right to demand that we file a registration statement or request that their shares be covered by a registration statement that we are otherwise filing.

Employment Agreements

See the “Executive Compensation—Employment Arrangements with Our Named Executive Officer” section of this Annual Report on Form 10-K for a further discussion of these arrangements.

Indemnification Agreements

Our certificate of provides that we will indemnify our directors and officers to the fullest extent permitted by Delaware law. In addition, we have entered and in the future plan to enter into indemnification agreements with each of our officers and directors that may be broader in scope than the specific indemnification provisions contained in the Delaware General Corporation Law. See “Executive Compensation—Limitations on Liability and Indemnification” for additional information regarding these agreements.

Policies and Procedures for Related Person Transactions

We have adopted a written related party transactions policy that such transactions must be approved by our audit committee. Pursuant to this policy, the audit committee has the primary responsibility for reviewing and approving or disapproving “related party transactions,” which are transactions between us and related persons in which the aggregate amount involved exceeds or may be expected to exceed $120,000 and in which a related person has or will have a direct or indirect material interest. For purposes of this policy, a related person will be defined as a director, executive officer, nominee for director, or greater than 5% beneficial owner of our common stock, in each case since the beginning of the most recently completed year, and their immediate family members. Our audit committee charter will provide that the audit committee shall review and approve or disapprove any related party transactions.

We did not have a written policy regarding the review and approval of related transactions prior to our IPO. Nevertheless, our board of directors reviewed and approved transactions with directors, officers and holders of 5% or more of our voting securities and their affiliates, each a related party. The material facts as to the related party’s relationship or interest in the transaction were disclosed to our board of directors prior to their consideration of such transaction, and the transaction was not considered approved by our board of directors unless a majority of the directors who were not interested

in the transaction approved the transaction. Further, when stockholders were entitled to vote on a transaction with a related party, the material facts of the related party's relationship or interest in the transaction were disclosed to the stockholders, who approved the transaction in good faith.

Director Independence

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

In December 2017, our board of directors undertook a review of the composition of our board of directors and its committees and the independence of each director. Based upon information requested from and provided by each director concerning his or her background, employment and affiliations, including family relationships, our board of directors has determined that Jonathan Silverstein, Paul Fonteyne and Lynne Sullivan are each an "independent director" as defined under applicable Nasdaq rules. In making such determination, our board of directors considered the relationships that each such non-employee director has with our company and all other facts and circumstances that our board of directors deemed relevant in determining his or her independence, including the beneficial ownership of our capital stock by each non-employee director. Mr. Schor is not an independent director under these rules because he is our President and Chief Executive Officer.

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

Board Committees

Audit Committee

The members of our audit committee are Chen Schor, David Steinberg and Lynne Sullivan, and Lynne Sullivan is the chair of the audit committee. Our audit committee's responsibilities will include:

- appointing, approving the compensation of, and assessing the independence of our registered public accounting firm;
- overseeing the work of our independent registered public accounting firm, including through the receipt and consideration of reports from that firm;
- reviewing and discussing with management and our independent registered public accounting firm our annual and quarterly consolidated financial statements and related disclosures;
- monitoring our internal control over financial reporting, disclosure controls and procedures and code of business conduct and ethics;
- overseeing our internal audit function, if any;

- discussing our risk assessment and risk management policies;
- establishing policies regarding hiring employees from our independent registered public accounting firm and procedures for the receipt and retention of accounting related complaints and concerns;
- meeting independently with our internal auditing staff, if any, our independent registered public accounting firm and management;
- reviewing and approving or ratifying any related person transactions; and
- preparing the audit committee report required by the SEC rules.

All audit and non-audit services, other than *de minimis* non-audit services, to be provided to us by our independent registered public accounting firm must be approved in advance by our audit committee. Our board of directors has determined that Lynne Sullivan is an "audit committee financial expert" as defined in applicable SEC rules and that each of the members of our audit committee possesses the financial sophistication required for audit committee members under Nasdaq rules. We believe that the composition of our audit committee will meet the requirements for independence under current Nasdaq and SEC rules and regulations. Under the applicable Nasdaq rules, a company listed in connection with its initial public offering is permitted to phase in its compliance with the independent audit committee requirements set forth in Marketplace Rule 5615(b)(1) on the same schedule as it is permitted to phase in its compliance with the independence audit committee requirement pursuant to Rule 10A-3(b)(1)(iv)(A) under the Exchange Act, that is, (1) one independent member at the time of listing; (2) a majority of independent members within 90 days of listing; and (3) all independent members within one year of listing.

The Audit Committee held two meetings during 2017. The Audit Committee operates under a written charter that satisfies the applicable standards of the SEC and Nasdaq. A copy of the Audit Committee charter is available on our website at http://ir.restorbio.com/corporate-governance/committee-composition.

Compensation Committee

The members of our compensation committee are Paul Fonteyne, Jonathan Silverstein and David Steinberg, and Paul Fonteyne is the chair of the compensation committee. Our compensation committee's responsibilities will include:

- reviewing and approving, or making recommendations to our board of directors with respect to, the compensation of our chief executive officer and our other executive officers;
- overseeing an evaluation of our senior executives;
- reviewing and making recommendations to our board of directors with respect to our incentive-compensation and equity-based compensation plans;
- overseeing and administering our equity-based plans;
- reviewing and making recommendations to our board of directors with respect to director compensation;
- reviewing and discussing annually with management our "Compensation Discussion and Analysis" disclosure if and to the extent then required by SEC rules; and
- preparing the compensation committee report if and to the extent then required by SEC rules.

Under the applicable Nasdaq rules, a company listing in conjunction with its initial public offering is permitted to phase in its compliance with the independent committee requirements set forth in Nasdaq Rules §5605(d) and (e) as follows: (1) one independent member at the time of listing; (2) a majority of independent members within 90 days of listing; and (3) all independent members within one year of listing.

The Compensation Committee held one meeting during 2017. The Compensation Committee operates under a written charter that satisfies the applicable standards of the SEC and Nasdaq. A copy of the Compensation Committee charter is available on our website at http://ir.restorbio.com/corporate-governance/committee-composition.

Nominating and Corporate Governance Committee

The members of our nominating and corporate governance committee are Paul Fonteyne, Jonathan Silverstein and Daphne Zohar, and Jonathan Silverstein is the chair of the nominating and corporate governance committee. Our nominating and corporate governance committee's responsibilities will include:

- identifying individuals qualified to become members of our board of directors;
- recommending to our board of directors the persons to be nominated for election as directors and to each of our board's committees;
- developing and recommending to our board of directors corporate governance principles; and
- overseeing an annual evaluation of our board of directors.

Under the applicable Nasdaq rules, a company listing in conjunction with its initial public offering is permitted to phase in its compliance with the independent committee requirements set forth in Nasdaq Rules §5605(d) and (e) as follows: (1) one independent member at the time of listing; (2) a majority of independent members within 90 days of listing; and (3) all independent members within one year of listing.

The Nominating and Corporate Governance Committee held one meeting during 2017. The Nominating and Corporate Governance Committee operates under a written charter that satisfies the applicable standards of the SEC and Nasdaq. A copy of the Nominating and Corporate Governance Committee charter is available on our website at http://ir.restorbio.com/corporate-governance/committee-composition.

Director Affiliations

Some of our directors are affiliated with and serve on our board of directors as representatives of entities which beneficially own or owned 5% or more of our common stock, as indicated below:

Name	Principal Stockholder
David Steinberg	PureTech Health LLC
Daphne Zohar	PureTech Health LLC
Jonathan Silverstein	OrbiMed Private Investments VI, LP

Item 14. Principal Accountant Fees and Services.

KPMG LLP provided audit services to the Company consisting of the audit of the Company's 2016 and 2017 consolidated financial statements. The following table summarizes the fees for KPMG LLP services to the Company for the last two fiscal years.

Fee Category	Fiscal Year 2017 ($)	Fiscal Year 2016 ($)
Audit Fees (1)	$ 582,116	$ —
Audit-Related Fees (2)	—	—
Tax Fees (3)	—	—
All Other Fees (4)	—	—
Total Fees	$ 582,116	$ —

(1) Audit fees consist of fees for the audit of our annual consolidated financial statements and fees related to our IPO.
(2) There were no audit-related fees for fiscal years 2017 and 2016.
(3) There were no tax fees for fiscal years 2017 and 2016.
(4) There were no other fees for fiscal years 2017 and 2016.

In 2018, the Audit Committee adopted a formal policy concerning approval of audit and non-audit services to be provided to the Company by its independent registered public accounting firm, KPMG LLP. The policy requires that all services to be provided by KPMG LLP, including audit services and permitted audit-related and non-audit services, must be preapproved by the Audit Committee, provided that de minimis non-audit services may instead be approved in accordance with applicable SEC rules. The Board of Directors preapproved all audit and non-audit services provided by KPMG LLP during fiscal year 2017 and fiscal year 2016.

PART IV

Item 15. Exhibits and Financial Statement Schedules.

(a) Financial Statements

The following financial statements and supplementary data are included in Item 8 of this Annual Report on Form 10-K.

Item 16. 10-K Summary

Not applicable.

EXHIBIT INDEX

Exhibit Number	Description of Exhibit
3.1	Third Amended and Restated Certificate of Incorporation of the Registrant (as currently in effect) (Incorporated by reference to Exhibit 3.1 to our Current Report filed with the SEC on January 30, 2018)
3.2	Amended and Restated Bylaws of the Registrant (as currently in effect) (Incorporated by reference to Exhibit 3.2 to our Current Report filed with the SEC on January 30, 2018)
4.1	Specimen stock certificate evidencing the shares of common stock (Incorporated by reference to Exhibit 4.1 to our Registration Statement on Form S-1/A filed with the SEC on January 16, 2018)
4.2	Amended and Restated Investors' Rights Agreement, dated as of November 29, 2017, among the Registrant and the other parties thereto (Incorporated by reference to Exhibit 4.1 to our Registration Statement on Form S-1 filed with the SEC on December 29, 2017)
10.1#	2017 Stock Incentive Plan and forms of award agreements thereunder (Incorporated by reference to Exhibit 10.1 to our Registration Statement on Form S-1 filed with the SEC on December 29, 2017)
10.2#	2018 Stock Incentive Plan and forms of award agreements thereunder (Incorporated by reference to Exhibit 10.2 to our Registration Statement on Form S-1/A filed with the SEC on January 16, 2018)
10.3#	Form of Director and Officer Indemnification Agreement (Incorporated by reference to Exhibit 10.3 to our Registration Statement on Form S-1/A filed with the SEC on January 16, 2018)
10.4#	Form of Officer Indemnification Agreement (Incorporated by reference to Exhibit 10.4 to our Registration Statement on Form S-1/A filed with the SEC on January 16, 2018)
10.5#	2018 Employee Stock Purchase Plan (Incorporated by reference to Exhibit 10.5 to our Registration Statement on Form S-1/A filed with the SEC on January 16, 2018)
10.6#	Non-Employee Director Compensation Policy (Incorporated by reference to Exhibit 10.6 to our Registration Statement on Form S-1/A filed with the SEC on January 16, 2018)
10.7+	License Agreement, dated as of March 23, 2017, by and between the Registrant and Novartis International Pharmaceutical Ltd. (Incorporated by reference to Exhibit 10.7 to our Registration Statement on Form S-1/A filed with the SEC on January 16, 2018)
10.8+	First Amendment to License Agreement, dated as of October 3, 2017, by and among the Registrant and Novartis International Pharmaceutical Ltd. (Incorporated by reference to Exhibit 10.5 to our Registration Statement on Form S-1 filed with the SEC on December 29, 2017)
10.9	Business Services, Personnel and Information Management Agreement, dated as of August 1, 2016, by and among the Registrant, PureTech Management, Inc., PureTech Health LLC and PureTech Health plc (Incorporated by reference to Exhibit 10.6 to our Registration Statement on Form S-1 filed with the SEC on December 29, 2017)
10.10#	Offer Letter, dated as of March 31, 2017, between the Registrant and Chen Schor (Incorporated by reference to Exhibit 10.7 to our Registration Statement on Form S-1 filed with the SEC on December 29, 2017)

Exhibit Number	Description of Exhibit
10.11#	Offer Letter, dated as of March 31, 2017, between the Registrant and Joan Mannick (Incorporated by reference to Exhibit 10.8 to our Registration Statement on Form S-1 filed with the SEC on December 29, 2017)
10.12#	Offer Letter, dated as of October 5, 2017, between the Registrant and John McCabe (Incorporated by reference to Exhibit 10.9 to our Registration Statement on Form S-1 filed with the SEC on December 29, 2017)
10.13#	Amendment to Offer Letter, dates as of March 31, 2017, between the Registrant and Joan Mannick (Incorporated by reference to Exhibit 10.13 to our Registration Statement on Form S-1/A filed with the SEC on January 16, 2018)
10.14#	Amendment to Offer Letter, dates as of March 31, 2017, between the Registrant and Chen Schor (Incorporated by reference to Exhibit 10.14 to our Registration Statement on Form S-1/A filed with the SEC on January 16, 2018)
10.15	Office Lease Agreement, dated as of January 8, 2018, by and between the Registrant and 500 Boylston and 222 Berkeley Owner (DE) LLC (Incorporated by reference to Exhibit 10.12 to our Registration Statement on Form S-1/A filed with the SEC on January 16, 2018)
10.16#*	Senior Executive Cash Incentive Bonus Plan
21.1*	Subsidiaries of the Registrant
23.1*	Consent of KPMG LLP, independent registered public accounting firm
31.1*	Rule 13a-14(a) Certification of Principal Executive Officer
31.2*	Rule 13a-14(a) Certification of Principal Financial Officer
32.1*	Certification of Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. §1350

* Filed herewith.

\+ Confidential treatment granted as to certain portions, which portions have been omitted and filed separately with the Securities and Exchange Commission.

\# Indicates a management contract or any compensatory plan, contract or arrangement.

SIGNATURES

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

resTORbio, Inc.

Date: March 29, 2018

By: /s/ Chen Schor
Chen Schor
President, Chief Executive Officer and Director
(Principal Executive Officer)

Pursuant to the requirements of the Securities Act of 1934, this Annual Report on Form 10-K has been signed by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Chen Schor Chen Schor	President, Chief Executive Officer and Director (principal executive officer)	March 29, 2018
/s/ John McCabe John McCabe	Vice President, Finance (principal financial officer and principal accounting officer)	March 29, 2018
/s/ Paul Fonteyne Paul Fonteyne	Director	March 29, 2018
/s/ Jonathan Silverstein Jonathan Silverstein	Director	March 29, 2018
/s/ David Steinberg David Steinberg	Director	March 29, 2018
/s/ Lynne Sullivan Lynne Sullivan	Director	March 29, 2018
/s/ Daphne Zohar Daphne Zohar	Director	March 29, 2018

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors

resTORbio, Inc.:

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of resTORbio, Inc. and subsidiaries (the Company) as of December 31, 2017 and 2016, the related consolidated statements of operations, redeemable convertible preferred stock and stockholders' (deficit) equity, and cash flows for the year ended December 31, 2017 and the period July 5, 2016 (inception) through December 31, 2016 and the related notes (collectively, the consolidated financial statements).

In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2017 and 2016, and the results of its operations and its cash flows for the year ended December 31, 2017 and the period July 5, 2016 (inception) through December 31, 2016, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

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

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud.

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

/s/ KPMG LLP

We have served as the Company's auditor since 2017.

Cambridge, Massachusetts
March 29, 2018

resTORbio, Inc.
Consolidated Balance Sheets
(In thousands, except share and per share data)

	December 31, 2017	December 31, 2016
Assets		
Current assets:		
Cash and cash equivalents	$ 53,349	$ —
Prepaid expenses	792	—
Deferred offering costs	929	—
Other current assets	84	—
Total current assets	55,154	—
Property and equipment, net	39	—
Total assets	$ 55,193	$ —
Liabilities, redeemable convertible preferred stock and stockholders' (deficit) equity		
Current liabilities:		
Accounts payable (including related party amounts of $32 and $0 as of December 31, 2017 and 2016, respectively)	$ 1,515	$ —
Accrued liabilities	3,987	—
Total current liabilities	5,502	—
Total liabilities	5,502	—
Commitments and contingencies (see Note 11)		
Redeemable convertible preferred stock:		
Redeemable convertible preferred stock, Series A, $0.0001 par value, 15,527,951 and no shares authorized as of December 31, 2017 and 2016, respectively; 15,527,951 and no shares issued and outstanding as of December 31, 2017 and 2016, respectively; aggregate liquidation preference of $30,000 and $0 as of December 31, 2017 and 2016, respectively	41,674	—
Redeemable convertible preferred stock, Series B, $0.0001 par value, 4,792,716 and no shares authorized as of December 31, 2017 and 2016, respectively; 4,792,716 and no shares issued and outstanding as of December 31, 2017 and 2016, respectively; aggregate liquidation preference of $40,000 and $0 as of December 31, 2017 and 2016, respectively	39,946	—
Stockholders' (deficit) equity:		
Common stock, $0.0001 par value, 30,000,000 and 7,000,000 shares authorized as of December 31, 2017 and 2016, respectively; 5,659,089 and 3,772,726 shares issued and outstanding as of December 31, 2017 and 2016, respectively; 4,562,640 and 2,082,860 shares vested as of December 31, 2017 and 2016, respectively	1	1
Additional paid-in capital	1,849	—
Accumulated deficit	(33,779)	(1)
Total stockholders' (deficit) equity	(31,929)	—
Total liabilities, redeemable convertible preferred stock and stockholders' (deficit) equity	$ 55,193	$ —

See accompanying notes to these consolidated financial statements.

resTORbio, Inc.
Consolidated Statements of Operations
(In thousands, except share and per share data)

	Year Ended December 31, 2017	July 5, 2016 (inception) through December 31, 2016
Operating expenses:		
Research and development	$ 16,839	$ —
General and administrative	2,043	1
Total operating expenses	18,882	1
Loss from operations	(18,882)	(1)
Other expense, net (see Note 7)	(14,896)	—
Loss before income taxes	(33,778)	(1)
Income tax expense	—	—
Net loss	$ (33,778)	$ (1)
Net loss per share, basic and diluted	$ (8.42)	$ (0.00)
Weighted-average common shares used in computing net loss per share, basic and diluted	4,009,513	1,978,137

See accompanying notes to these consolidated financial statements.

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

	Series A Redeemable Convertible Preferred Stock		Series B Redeemable Convertible Preferred Stock		Common Stock		Additional Paid In	Accumulated	Shareholders (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount	Capital	Deficit	Equity
Balance at July 5, 2016	—	$ —	—	$ —	—	$ —	$ —	$ —	$ —
Vesting of restricted shares	—	—	—	—	2,082,860	1	—	—	1
Net loss	—	—	—	—	—	—	—	(1)	(1)
Balance at December 31, 2016	—	$ —	—	$ —	2,082,860	$ 1	$ —	$ (1)	$ —
Issuance of common shares to PureTech (see Note 13)	—	—	—	—	1,886,363	—	—	—	—
Issuance of Series A redeemable convertible preferred stock, net of tranche liability	15,527,951	41,674	—	—	—	—	1,379	—	1,379
Issuance of Series B redeemable convertible preferred stock, net of issuance costs of $54	—	—	4,792,716	39,946	—	—	—	—	—
Vesting of restricted shares	—	—	—	—	593,417	—	—	—	—
Stock-based compensation expense	—	—	—	—	—	—	470	—	470
Net loss	—	—	—	—	—	—	—	(33,778)	(33,778)
Balance at December 31, 2017	15,527,951	$ 41,674	4,792,716	$ 39,946	4,562,640	$ 1	$ 1,849	$ (33,779)	$ (31,929)

See accompanying notes to these consolidated financial statements.

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

	Year Ended December 31, 2017	July 5, 2016 (inception) through December 31, 2016
Operating activities:		
Net loss	$ (33,778)	$ (1)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization expense	5	—
Stock-based compensation expense	470	—
Change in fair value of tranche rights (see Note 7)	14,896	—
Expense related to acquisition of intellectual property (see Note 6)	3,157	—
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(876)	—
Accounts payable	1,392	—
Accrued liabilities	3,749	1
Net cash used in operating activities	(10,985)	—
Investing activities:		
Purchases of property and equipment	(44)	—
Net cash used in investing activities	(44)	—
Financing activities:		
Proceeds from issuance of Series A redeemable convertible preferred stock	25,000	—
Proceeds from issuance of Series B redeemable convertible preferred stock, net	39,946	—
Deferred offering costs	(568)	—
Net cash provided by financing activities	64,378	—
Net increase in cash and cash equivalents	53,349	—
Cash and cash equivalents at beginning of period	—	—
Cash and cash equivalents at end of period	$ 53,349	$ —

See accompanying notes to these consolidated financial statements.

1. Organization

resTORbio, Inc. ("the Company") was incorporated in the State of Delaware on July 5, 2016. The Company is a clinical-stage biopharmaceutical company focused on the development and commercialization of novel therapeutics for the treatment of aging-related diseases and conditions. The Company's principal operations are located in Boston, Massachusetts.

Since inception, the Company has been primarily involved in research and development activities. The Company devotes substantially all of its efforts to product research and development, initial market development and raising capital. The Company has not generated any product revenue related to its primary business purpose to date and is subject to a number of risks similar to those of other early stage companies, including dependence on key individuals, competition from other companies, the need for development of commercially viable products and the need to obtain adequate additional financing to fund the development of its product candidates. The Company is also subject to a number of risks similar to other companies in the life sciences industry, including regulatory approval of products, uncertainty of market acceptance of products, competition from substitute products and larger companies, the need to obtain additional financing, compliance with government regulations, protection of proprietary technology, dependence on third parties, product liability and dependence on key individuals.

Initial Public Offering

On January 30, 2018, the Company completed its initial public offering ("IPO"), whereby the Company sold 6,516,667 shares of its common stock (inclusive of 850,000 shares of common stock sold by the Company pursuant to the full exercise of an overallotment option granted to the underwriters in connection with the offering) at a price of $15.00 per share. The shares began trading on The Nasdaq Global Select Market on January 26, 2018. The aggregate net proceeds received by the Company from the offering were approximately $89.4 million, after deducting underwriting discounts and commissions and other offering expenses payable by the Company. As of December 31, 2017, the Company had incurred $0.9 million of costs related to the IPO which have been deferred. Upon the closing of the IPO, all outstanding shares of redeemable convertible preferred stock converted into 15,870,559 shares of common stock and all unvested shares of restricted stock automatically vested. Additionally, the Company is now authorized to issue 150,000,000 shares of common stock and 10,000,000 shares of preferred stock.

Liquidity

In the course of its development activities, the Company has sustained operating losses and expects such losses to continue over the next several years. The Company's ultimate success depends on the outcome of its research and development activities. The Company has incurred net losses from operations since inception and has an accumulated deficit of $33.8 million as of December 31, 2017. On January 30, 2018, the Company completed its IPO whereby the Company sold 6,516,667 shares of its common stock for aggregate net proceeds of approximately $89.4 million. The Company believes that its cash and cash equivalents, together with the proceeds from the IPO, will be sufficient to fund the Company's current operating plan through at least the next twelve months.

2. Summary of Significant Accounting Policies

Basis of Presentation and Use of Estimates

The accompanying consolidated financial statements have been prepared in accordance with U.S. generally accepted accounting principles ("U.S. GAAP"). The Company's fiscal year end is December 31st. Any reference in these notes to applicable guidance is meant to refer to the authoritative United States generally accepted accounting principles as found in the Accounting Standards Codification ("ASC") and Accounting Standards Updates ("ASUs") of the Financial Accounting Standards Board ("FASB"). The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities, as of the date of the consolidated financial statements, and the reported amounts of any expenses during the reporting period. On an ongoing basis, management evaluates its estimates, including those related to accrued liabilities, fair value of tranche liabilities, fair value of common stock, income taxes, and stock-based compensation expense. Management bases its estimates on historical experience, and on various other market-specific relevant assumptions that management believes to be reasonable, under the circumstances. Actual results may differ from those estimates or assumptions.

The consolidated financial statements include the accounts of resTORbio, Inc. and its wholly owned subsidiary, resTORbio Securities Corp. All inter-company transactions and balances have been eliminated in consolidation.

Fair Value Measurements

Fair value is defined as the price at which an asset could be exchanged in a current transaction between knowledgeable, willing parties. A liability's fair value is defined as the amount that would be paid to transfer the liability to a new obligor, not the amount that would be paid to settle the liability with the creditor. Where available, fair value is based on observable market prices, or parameters derived from such prices. Where observable prices or inputs are not available, valuation models are applied. These valuation techniques involve some level of management estimation and judgment. The degree of management estimation and judgment is dependent on the price transparency for the instruments, or market, and the instruments' complexity. The authoritative accounting guidance describes a fair value hierarchy based on three levels of inputs that may be used to measure fair value, of which the first two are considered observable and the last is considered unobservable. These levels of inputs are as follows:

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

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

Level 3—Unobservable inputs that reflect management's best estimate of what market participants would use in pricing the asset or liability at the measurement date. Consideration is given to the risk inherent in the valuation technique and the risk inherent in the inputs to the model.

To the extent that valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

Financial instruments measured at fair value on a recurring basis include the tranche rights associated with the redeemable convertible preferred stock (Note 7). The fair value of the tranche rights were determined based on Level 3 inputs as described in Note 7. An entity may elect to measure many financial instruments and certain other items at fair value at specified election dates. Subsequent unrealized gains and losses on items for which the fair value option has been elected will be reported in net loss. The Company did not elect to measure any additional financial instruments or other items at fair value.

There have been no changes to the valuation methods utilized by the Company during the year ended December 31, 2017 and the period from July 5, 2016 (inception) to December 31, 2016. The Company evaluates transfers between levels at the end of each reporting period. There were no transfers of financial instruments between levels during the year ended December 31, 2017 and the period from July 5, 2016 (inception) to December 31, 2016.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to a concentration of credit risk consist of cash and cash equivalents. The Company's cash and cash equivalents are held by financial institutions in the United States. Amounts on deposit may at times exceed federally insured limits. Management believes that the financial institution is financially sound, and accordingly, minimal credit risk exists with respect to the financial institution.

Concentration of Manufacturing Risk

As of December 31, 2017, the Company had manufacturing arrangements with vendors for the supply of materials for use in preclinical and clinical studies. If the Company were to experience any disruptions in either party's ability or willingness to continue to provide manufacturing services, the Company may experience significant delays in its product development timelines and may incur substantial costs to secure alternative sources of manufacturing.

Property and Equipment

Property and equipment are stated at cost, less accumulated depreciation. Depreciation is recorded using the straight-line method over the estimated useful lives of the respective assets. Depreciation begins at the time the asset is placed in service. Maintenance and repairs that do not improve or extend the lives of the respective assets are expensed to operations as incurred. Upon sale or retirement of assets, the cost and related accumulated depreciation are removed from the consolidated balance sheet and the resulting gain or loss is reflected in the consolidated statements of operations.

The estimated useful lives of property and equipment are as follows:

	Useful Life (in years)
Laboratory and manufacturing equipment	2-8 years
Computer equipment and software	1-5 years

Impairment of Long-Lived Assets

The Company evaluates its long-lived assets, including property and equipment, for impairment whenever events or changes in circumstances indicate that the carrying value of these assets may not be recoverable. Recoverability of these assets is measured by comparison of the carrying amount of each asset to the future undiscounted cash flows the asset is expected to generate over its remaining life. If the asset is considered to be impaired, the amount of any impairment is measured as the difference between the carrying value and the fair value of the impaired asset. The Company has recorded no impairment of any long-lived assets during any of the periods presented.

Accrued Research and Development Costs

The Company accrues for estimated costs of research and development activities conducted by third-party service providers, which include the conduct of preclinical studies and clinical trials, and contract manufacturing activities. The Company records the estimated costs of research and development activities based upon the estimated amount of services provided, and includes these costs in accrued liabilities in the consolidated balance sheets and within research and development expenses in the consolidated statements of operations. These costs are a significant component of the Company's research and development expenses. The Company accrues for these costs based on factors such as estimates of the work completed and in accordance with agreements established with its third-party service providers. The Company estimates the amount of work completed by its third-party service providers through discussions with internal personnel and external service providers as to the progress or stage of completion of the services and the agreed-upon fee to be paid for such services. The majority of the Company's service providers invoice in arrears for services performed, on a pre-determined schedule or when contractual milestones are met; however, some require advance payments. The Company makes significant judgments and estimates in determining the accrued balance in each reporting period based on the facts and circumstances known at that time. As actual costs become known, the Company adjusts its accrued estimates. Although the Company does not expect its estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed, the number of patients enrolled and the rate of patient enrollment may vary from its estimates and could result in us reporting amounts that are too high or too low in any particular period. The Company's accrued expenses are dependent, in part, upon the receipt of timely and accurate reporting from CROs, CMOs and other third-party service providers. To date, there have been no material differences from its accrued expenses to actual expenses.

Research and Development Costs

Research and development costs are expensed as incurred and consist of personnel costs, lab supplies and other costs, as well as fees paid to third parties to conduct research and development activities on the Company's behalf. Amounts incurred in connection with license agreements are also included in research and development expenses. The Company records payments made to outside vendors for services performed or goods being delivered for use in research and development activities as either prepaid expenses or accrued expenses, depending on the timing of when services are performed or goods are delivered.

Equity-Based Compensation Expense

The Company recognizes equity-based compensation expense for awards of equity instruments to employees and non-employees based on the grant date fair value of those awards in accordance with FASB ASC Topic 718, *Stock Compensation* ("ASC 718"). ASC 718 requires all equity-based compensation awards to employees and non-employee directors, including grants of restricted shares and stock options, to be recognized as expense in the consolidated statements

of operations based on their grant date fair values. The Company estimates the fair value of stock options using the Black-Scholes option pricing model. The Company uses the value of its common stock to determine the fair value of restricted shares.

The Company accounts for restricted stock and common stock options issued to non-employees under FASB ASC Topic 505-50, *Equity- Based Payments to Non-Employees* ("ASC 505-50"). As such, the value of such options is periodically remeasured and income or expense is recognized over their vesting terms. Compensation cost related to awards with service-based vesting schedules is recognized using the straight-line method. The Company determines the fair value of the restricted stock and common stock granted to non-employees as either the fair value of the consideration received or the fair value of the equity instruments issued.

The Black-Scholes option pricing model requires the input of certain subjective assumptions, including (i) the expected share price volatility, (ii) the expected term of the award, (iii) the risk-free interest rate and (iv) the expected dividend yield. Due to the lack of a public market for the trading of the Company's common stock and a lack of company-specific historical and implied volatility data, the Company has based its estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. The historical volatility is calculated based on a period of time commensurate with the expected term assumption. The group of representative companies have characteristics similar to the Company, including stage of product development and focus on the life science industry. The Company uses the simplified method, which is the average of the final vesting tranche date and the contractual term, to calculate the expected term for options granted to employees as it does not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. For options granted to non-employees, the Company utilizes the contractual term of the arrangement as the basis for the expected term assumption. The risk-free interest rate is based on a treasury instrument whose term is consistent with the expected term of the stock options. The Company uses an assumed dividend yield of zero as the Company has never paid dividends and has no current plans to pay any dividends on its common stock.

The Company expenses the fair value of its equity-based compensation awards granted to employees on a straight-line basis over the associated service period, which is generally the period in which the related services are received. The Company measures equity-based compensation awards granted to non-employees at fair value as the awards vest and recognizes the resulting value as compensation expense at each financial reporting period. The Company accounts for award forfeitures as they occur.

Determination of Fair Value of Common and Preferred Shares and Tranche Rights Liability

Prior to the completion of the Company's IPO, the Company was required to estimate the fair value of its common stock underlying its stock-based awards when performing the fair value calculations using the Black-Scholes option pricing model. The estimated fair value of the Company's common and preferred shares has been determined by the board of directors as of the grant date, with input from management, considering the Company's most recently available third-party valuations of common shares and the board of directors' assessment of additional objective and subjective factors that it believed were relevant and which may have changed from the date of the most recent valuation through the date of the grant. These third-party valuations were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*. The Company's common and preferred share valuations were prepared using either an option-pricing method, or OPM, or a probability-weighted expected return method, or PWERM, which uses a combination of market approaches and an income approach to estimate the Company's enterprise value. The OPM treats common securities and preferred securities as call options on the total equity value of a company, with exercise prices based on the value thresholds at which the allocation among the various holders of a company's securities changes. Under this method, the common and preferred shares have value only if the funds available for distribution to members are expected to exceed the value of the preferred security liquidation preference at the time of the liquidity event, such as a strategic sale or a merger. The PWERM is a scenario-based methodology that estimates the fair value of common and preferred shares based upon an analysis of future values for the enterprise, assuming various outcomes. The common and preferred share values are based on the probability-weighted present value of expected future investment returns considering each of the possible outcomes available as well as the rights of each class of common and preferred securities. The future value of the common and preferred shares under each outcome is discounted back to the valuation date at an appropriate risk-adjusted discount rate and probability weighted to arrive at an indication of value for the common and preferred shares. The estimated fair value of the tranche rights was determined using the difference between the total purchase price of the Company's preferred stock and the total fair value of the preferred stock using a risk-adjusted forward contract model.

Income Taxes

The Company uses the asset and liability method of accounting for income taxes in accordance with FASB ASC Topic 740, *Income Taxes*. Under this method, deferred tax assets and liabilities are determined based on the differences between the financial reporting and the tax basis of assets and liabilities, and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. The Company must then assess the likelihood that the resulting deferred tax assets will be realized. A valuation allowance is provided when it is more likely than not that some portion, or all of a deferred tax asset will not be realized. Due to the Company's lack of earnings history, the net deferred tax assets have been fully offset by a valuation allowance.

The Company recognizes benefits of uncertain tax positions if it is more likely than not that such positions will be sustained upon examination based solely on their technical merits, as the largest amount of benefit that is more likely than not to be realized upon the ultimate settlement. The Company's policy is to recognize interest and penalties related to the underpayment of income taxes as a component of income tax expense or benefit. To date, the Company has no uncertain tax positions and there have been no interest charges or penalties related to unrecognized tax benefits.

Net Loss per Share

Basic net loss per share is calculated by dividing the net loss by the weighted average number of shares of common stock outstanding during the period without consideration of common stock equivalents. Diluted net loss per common share is the same as basic net loss per common share for all periods presented, since the effects of potentially dilutive securities are antidilutive.

Recently Adopted Accounting Pronouncements

In August 2014, the FASB issued ASU 2014-15, *Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern* ("ASU 2014-15"). ASU 2014-15 requires management to evaluate relevant conditions, events, and certain management plans that are known or reasonably knowable that, when considered in the aggregate, raise substantial doubt about the entity's ability to continue as a going concern within one year after the date that the financial statements are issued, for both annual and interim periods. ASU 2014-15 also requires certain disclosures around management's plans and evaluation, as well as the plans, if any, that are intended to mitigate those conditions or events that will alleviate the substantial doubt. ASU 2014-15 is effective for fiscal years ending after December 15, 2016. The Company adopted this guidance on July 5, 2016 (inception).

In March 2016, the FASB issued ASU No. 2016-09, *Compensation—Stock Compensation (Topic 718)* ("ASU 2016-09"). The guidance changes how companies account for certain aspects of equity-based payments to employees. Entities will be required to recognize income tax effects of awards in the income statement when the awards vest or are settled. The guidance also allows an employer to repurchase more of an employee's shares than it can under current guidance for tax withholding purposes providing for withholding at the employee's maximum rate as opposed to the minimum rate without triggering liability accounting and to make a policy election to account for forfeitures as they occur. The updated guidance is effective for annual periods beginning after December 15, 2017. Early adoption is permitted. The Company adopted this guidance on July 5, 2016 (inception) and made the policy election to account for forfeitures as they occur. No awards have been forfeited as of December 31, 2017.

Recently Issued Accounting Pronouncements

In November 2016, the FASB issued ASU 2016-18, *Statement of Cash Flows* ("ASU 2016-18"), which requires that amounts generally described as restricted cash and restricted cash equivalents should be included with cash and cash equivalents when reconciling the beginning-of-period and end-of-period total amounts shown on the statement of cash flows. ASU 2016-18 is effective for fiscal years beginning after December 15, 2018 and should be applied using a retrospective transition method to each period presented. Early adoption is permitted. The Company does not expect the impact of ASU 2016-18 to be material to its consolidated financial statements.

In May 2017, the FASB issued ASU 2017-09, *Compensation—Stock Compensation* (Topic 718): Scope of Modification Accounting ("ASU 2017-09"). ASC 2017-09 provides guidance about which changes to the terms or conditions of a share-based payment award require an entity to apply modification accounting in Topic 718. The guidance is effective for annual periods beginning after December 15, 2017, with early adoption permitted, including adoption in any interim period for which financial statements have not yet been issued. The Company is currently evaluating the potential effects of adopting the provisions of ASU 2017-09.

In July 2017, the FASB issued ASU 2017-11, *Accounting for Certain Financial Instruments with Down Round Features* ("ASU 2017-11"), which updates the guidance related to the classification analysis of certain equity-linked financial instruments (or embedded features) with down round features. Under ASU 2017-11, a down round feature no longer precludes equity classification when assessing whether the instrument is indexed to an entity's own stock. As a result, a freestanding equity-linked financial instrument (or embedded conversion option) no longer would be accounted for as a derivative liability at fair value as a result of the existence of a down round feature. For freestanding equity classified financial instruments, the amendments require entities that present earnings per share (EPS) in accordance with Topic 260 to recognize the effect of the down round feature when it is triggered. That effect is treated as a dividend and as a reduction of income available to common shareholders in basic EPS. ASU 2017-11 is effective for public entities for all annual and interim periods beginning after December 15, 2019. Early adoption is permitted. The Company is currently evaluating the impact that the adoption of ASU 2017-11 will have on its consolidated financial statements.

3. Financial Instruments

There were no assets or liabilities measured at fair value as of December 31, 2017 and 2016. The Company did measure the fair value of the tranche rights from their issuance to settlement (See Note 7).

4. Property and equipment, net

Property and equipment, net consists of the following:

	As of December 31, 2017	2016
	(In thousands)	
Laboratory and manufacturing equipment	$ 38	$ —
Computer equipment and software	6	—
Total property and equipment	44	—
Less: accumulated depreciation	(5)	—
Property and equipment, net	$ 39	$ —

Depreciation expense was $5,000 and $0 for the year ended December 31, 2017 and the period from July 5, 2016 (inception) to December 31, 2016, respectively.

5. Accrued Liabilities

Accrued liabilities consist of the following:

	As of December 31, 2017	2016
	(In thousands)	
Accrued payroll and related expenses	$ 394	$ —
Accrued research and development expenses	3,250	—
Deferred offering costs	238	—
Other	105	—
Total accrued liabilities	$ 3,987	$ —

6. License Agreements

Novartis License Agreement

On March 23, 2017, the Company entered into an exclusive license agreement with Novartis International Pharmaceutical Ltd. ("Novartis"). Under the agreement, Novartis granted the Company an exclusive, field-restricted, worldwide license, to certain intellectual property rights owned or controlled by Novartis, to develop, commercialize and sell one or more therapeutic products comprising RTB101 or RTB101 in combination with everolimus in a fixed dose combination. The exclusive field under the license agreement is for the treatment, prevention and diagnosis of disease and other conditions in all indications in humans and animals.

As initial consideration for the licensed rights, the Company issued Novartis Institutes for Biomedical Research ("NIBR") 2,587,992 shares of the Company's Series A Preferred Stock. The fair value of the Novartis license was $3.2 million based on the fair value of the Series A Preferred Stock which was determined to be $1.22 per share based on an independent third-party valuation, and is recorded as research and development expenses in the consolidated statements of operations.

The agreement may be terminated by either party upon a material breach by the other party that is not cured within 60 days after written notice. The Company may terminate the agreement in its entirety or on a product-by-product or country-by-country basis with or without cause with 60 days' prior written notice.

Novartis may terminate the portion of the agreement related to everolimus if the Company fails to use commercially reasonable efforts to research, develop and commercialize a product utilizing everolimus for a period of three years. Novartis may terminate the license agreement upon the Company's bankruptcy, insolvency, dissolution or winding up.

As additional consideration for the license, the Company is required to pay up to an aggregate of $4.3 million upon the satisfaction of clinical milestones, up to an aggregate of $24 million upon the satisfaction of regulatory milestones for the first indication approved, and up to an aggregate of $18 million upon the satisfaction of regulatory milestones for the second indication approved. In addition, the Company is required to pay up to an aggregate of $125 million upon the satisfaction of commercial milestones, based on the amount of annual net sales. The Company is also required to pay tiered royalties ranging from a mid single-digit percentage to a low teen-digit percentage on annual net sales of products. These royalty obligations last on a product-by-product and country-by-country basis until the latest of (i) the expiration of the last valid claim of a Novartis patent covering a subject product, (ii) the expiration of any regulatory exclusivity for the subject product in a country, or (iii) the 10th anniversary of the first commercial sale in the country, and are subject to a reduction after the expiration of the last valid claim of a Novartis patent or the introduction of a generic equivalent of a product in a country. In addition, if the Company sublicenses the rights under the license agreement, the Company is required to pay a certain percentage of sublicense revenue to Novartis. Novartis will no longer be entitled to sublicense revenue following the last visit of the 400th subject in any human clinical trial conducted by the Company or a sublicensee of the Company.

Milestone payments to Novartis will be recorded as research and development expenses in the consolidated statements of operations once achievement of each associated milestone has occurred or the achievement is considered probable. In May 2017, the Company initiated a Phase 2b clinical trial for a first indication, triggering the first milestone payment under the agreement. Accordingly, the Company paid the related $0.3 million payment in May 2017. As of December 31, 2017, none of the remaining development milestones, regulatory milestones, sales milestones, or royalties had been reached or were probable of achievement.

7. Redeemable Convertible Preferred Stock

As of December 31, 2017, the Company had 20,320,667 shares of preferred stock authorized, of which 15,527,951 shares were issued and outstanding and were designated as $0.0001 par value Series A Preferred Stock and 4,792,716 shares were issued and outstanding and were designated as $0.0001 par value Series B Preferred Stock.

The Company's redeemable convertible preferred shares have been classified as temporary or mezzanine equity on the accompanying consolidated balance sheets in accordance with U.S. GAAP for the classification and measurement of redeemable securities as the Series A and Series B Preferred Stock are contingently redeemable at the option of the holder for reasons outside of the Company's control. As of December 31, 2017, there has been no accretion of the redeemable convertible preferred shares to redemption value as at that date the shares are not redeemable or probable of being redeemed.

On March 23, 2017, the Company entered into a Series A Preferred Stock Purchase Agreement with PureTech Health LLC ("PureTech") and NIBR. Under the agreement, in the initial March 2017 closing, PureTech purchased 2,846,791 shares of Series A Preferred Stock at a purchase price of $1.932 per share, resulting in aggregate gross proceeds of $5.5 million, and NIBR was issued 2,587,992 shares of Series A Preferred Stock as consideration for an exclusive, field-restricted, worldwide license, to certain intellectual property rights owned or controlled by Novartis, to develop, commercialize and sell one or more therapeutic products comprising RTB101, alone or in combination with everolimus in a fixed dose combination (See Note 6). PureTech also agreed to purchase up to 4,917,185 additional shares, for total aggregate gross proceeds of $9.5 million (the "Tranche Rights"), at $1.932 per share at separate second and third closings to take place upon the occurrence of certain events as specified under the agreement. The fair value of the Series A Preferred Stock on the date of issuance was determined to be $1.22 per share based on an independent third-party valuation.

On March 23, 2017, the Company also entered into a side letter with PureTech under which PureTech agreed to purchase up to 5,175,984 additional shares at $1.932 per share at a fourth closing to take place on a future date based on the occurrence of certain events as specified under the letter. The Series A Tranche Rights were evaluated under ASC 480 – *Distinguishing Liabilities from Equity* and it was determined that they met the requirements for separate accounting from the initial issuance of Series A Preferred Stock as freestanding financial instruments and are accounted for as liabilities. The Company adjusts the carrying value of the Series A Tranche Rights to its estimated fair value at each reporting date up to the closing of each tranche financing. Increases or decreases in fair value of the Tranche Rights are recorded as other income (expense) in the consolidated statements of operations.

At the date of issuance, $2.0 million of the Series A Preferred Stock proceeds was allocated to the Series A Tranche Rights liability, which was recorded as a current liability on the consolidated balance sheets.

In September 2017, under the Series A Tranche Rights, the Company received gross proceeds of $4.5 million in exchange for the issuance of 2,329,193 shares of Series A Preferred Stock at $1.932 per share pursuant to the second closing on August 29, 2017. The fair value of the Series A Preferred Stock on the date of issuance was determined to be $1.34 per share based on an independent third-party valuation and the fair value of the Series A Tranche Rights liability was revalued to its estimated fair value of $1.4 million, resulting in other income of $0.6 million.

On October 12, 2017, the Company amended the Series A Preferred Stock Purchase Agreement to accelerate the third and fourth closings under the original agreement. The Company issued 7,763,975 shares of Series A Preferred Stock at $1.932 per share for aggregate gross proceeds of $15.0 million, of which $9.0 million was from PureTech and $6.0 million from a new investor. The fair value of the Series A Preferred Stock on the date of issuance was determined to be $4.11 per share based on an independent third-party valuation and the fair value of the Series A Tranche Rights liability was revalued to its estimated fair value of $10.1 million, resulting in other expense of $8.8 million. Following this closing of the Series A Preferred Stock financing, the Series A Tranche Rights have been terminated.

In connection with the October 12, 2017 Series A closing, the new investor entered into a commitment to purchase up to $20 million dollars of Series B Preferred Stock at a purchase price of $8.346 (the “Series B Tranche Right”). The new investor’s commitment to purchase Series B Preferred Stock was also determined to meet the requirements for separate accounting. The Series B Tranche Right was determined to be a freestanding financial instrument accounted for as an asset. On October 12, 2017, $6.8 million of the Series A Preferred Stock proceeds were allocated to this liability.

On October 27, 2017, the Company entered into the Series B Preferred Stock Agreement for the issuance and sale of up to 4,792,716 shares of Series B Preferred Stock at $8.346 per share. On November 29, 2017, the Company issued and sold 4,792,716 shares of Series B Preferred Stock at $8.346 per share for aggregate gross proceeds of $40.0 million (the “Series B Financing”), of which $20.0 million satisfied the series B Tranche Right.

The Company measured the fair value of the tranche rights liabilities/assets from issuance on March 23, 2017 to settlement on November 29, 2017. The tranche rights liabilities/assets are considered a Level 3 liability because its fair value measurement is based, in part, on significant inputs not observed in the market. Any reasonable changes in the assumptions used in the valuation could materially affect the financial results of the Company.

The following is a summary of the changes in fair value of the tranche rights and the impact on the consolidated financial statements:

	(In thousands)	Financial statement impacted
Beginning Balance, January 1, 2017	$ —	
Establishment of Series A tranche right liability on March 23, 2017	2,014	Consolidated balance sheets
Change in fair value of Series A tranche right liability immediately prior to second closing on September 8, 2017	(605)	Consolidated statements of operations
Mark-to-market of Series A tranche rights liability at September 30, 2017	(30)	Consolidated statements of operations
Change in fair value of tranche right liability immediately prior to final closing of the Series A on October 12, 2017	8,767	Consolidated statements of operations
Settlement of Series A tranche right liability upon closing of Series A on October 12, 2017	(10,146)	Consolidated balance sheets
Establishment of Series B tranche right asset on October 23, 2017	6,764	Consolidated statements of operations
Settlement of Series B tranche right asset upon closing of Series B on November 29, 2017	(6,764)	Consolidated balance sheets
Ending Balance, December 31, 2017	$ —	

The change in the fair value of the tranche rights is influenced primarily by the price of the underlying Series A and Series B Preferred Stock. The net change in fair value of $14.9 million for the year ended December 31, 2017 was recorded as other expense in the accompanying consolidated statements of operations.

The rights, privileges, and preferences of convertible preferred stock are summarized as follows:

Liquidation Preference

In the event of any voluntary or involuntary liquidation, dissolution, or winding up of the Company, or Deemed Liquidation Event (as defined below), the holders of shares of Series B Preferred Stock then outstanding shall be entitled to be paid out of the assets of the Corporation available for distribution to its stockholders before any payment shall be made to the holders of Series A Preferred Stock or Common Stock by reason of their ownership thereof, an amount per share equal to the Series B Original Issue Price of $8.346, plus any dividends declared and unpaid thereon. Then, the holders of shares of Series A Preferred Stock then outstanding shall be entitled to be paid out of the assets of the Company available for distribution to its stockholders before any payment shall be made to the holders of common stock, an amount per share equal to the Series A Original Issue Price of $1.932, plus any dividends declared and unpaid thereon. If upon any liquidation, dissolution, winding up of the Company or Deemed Liquidation Event, the assets of the Company available for distribution to shareholders is insufficient to pay the holders of shares of Series B Preferred Stock the full amount to which they shall be entitled, the holders of Series B Preferred Stock will share ratably in any distribution of the assets available for distribution in proportion to the respective amounts which would otherwise be payable in respect of the shares held by them upon such distribution if all amounts payable on or with respect to such shares were paid in full.

If upon any liquidation, dissolution, winding up of the Company or Deemed Liquidation Event, the assets of the Company available for distribution to shareholders is insufficient to pay the holders of shares of Series A Preferred Stock the full amount to which they shall be entitled, the holders of Series A Preferred Stock will share ratably in any distribution of the assets available for distribution in proportion to the respective amounts which would otherwise be payable in respect of the shares held by them upon such distribution if all amounts payable on or with respect to such shares were paid in full.

After payment of all preferential amounts required to be paid to the holders of preferred stock, the remaining funds and assets available for distribution to the shareholders of the Company will be distributed among the holders of preferred stock and common stock, pro rata based on the number of shares held by each such holder.

The following events are defined as Deemed Liquidation Events unless the holders of a majority of the then outstanding shares of preferred stock elect otherwise by written notice to the Company:

(i) a merger or consolidation; or

(ii) the sale, lease, transfer, exclusive license or other disposition, in a single transaction or series of related transactions, by the Company of all or substantially all the assets or intellectual property of the Company.

Voting

Each holder of shares of preferred stock is entitled to the number of votes equal to the number of whole shares of common stock into which such shares of preferred stock could be converted and has voting rights and powers equal to the voting rights and powers of the common stock, and except as provided by law or by other provisions of the Certificate of Incorporation, shall vote together with the common stock as a single class on an as-converted basis on all matters as to which holders of common stock have the right to vote.

The holders of Series A Preferred Stock, exclusively and as a separate class, are entitled to elect two members of the Company's board of directors and the holders of Series B Preferred Stock, exclusively and as a separate class, are entitled to elect one member of the Company's board of directors. The holders of common stock, exclusively and as a separate class, are entitled to elect two members of the Company's board of directors.

Redemption

The preferred stock may be redeemed upon a Deemed Liquidation Event. The Series A and Series B Preferred Stock may be redeemed at $1.932 and $8.346 per share, respectively, or the holders of preferred stock may receive an amount equal to the amount entitled if the preferred stock converted into shares of common stock on a 1.2804:1 basis on the redemption date; provided however, that no shares of Series A Preferred Stock may be redeemed until all shares of Series B Preferred Stock have been redeemed. At December 31, 2017, the shares of preferred stock were not redeemable and the likelihood of an occurrence of a Deemed Liquidation Event was not deemed to be probable.

Conversion

The holders of preferred stock are subject to certain optional and mandatory conversion rights.

(i) *Optional Conversion Rights:* Each share of convertible preferred stock is convertible, at the option of the holder, into such number of fully paid shares of common stock as is determined by dividing the original issuance price by the conversion price in effect at the time of conversion. As of December 31, 2017, the conversion ratio was 1.2804:1 for the preferred stock.

(ii) *Mandatory Conversion Rights:* Upon either (a) the closing of the sale of shares of common stock to the public at a price of at least $7.421 per share (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the common stock), in a firm-commitment underwritten public offering pursuant to an effective registration statement resulting in at least $25 million of gross proceeds to the Company or (b) the date and time, or the occurrence of an event, specified by vote or written consent of the holders of a majority of the then outstanding shares of preferred stock, then all outstanding shares of preferred stock shall automatically be converted into shares of common stock, at the then effective conversion rate.

The conversion price for preferred stock is subject to adjustment upon certain events including certain dilutive issuances of shares, share subdivisions such as stock splits and stock dividends, combinations, or other similar recapitalizations with respect to the common stock, or other similar events. At December 31, 2017 the Series A Preferred Stock had an original issuance price of $1.932 per share and a conversion price of $2.474. At December 31, 2017 the Series B Preferred Stock had an original issuance price of $8.346 per share and a conversion price of $10.686.

Dividends

If the Company declares or makes any dividends to holders of common stock of the Company, each holder of preferred stock shall be entitled to receive such dividend on an as-converted basis. Such dividends shall not accrue and shall not accumulate. No dividends had been declared as of December 31, 2017.

8. Common Stock

General

The voting, dividend and liquidation rights of the holders of common stock are subject to and qualified by the rights, powers, and preferences of the holders of the shares of preferred stock. The common stock has the following characteristics:

Voting

The holders of the common stock are entitled to one vote for each share of common stock held at all meetings of stockholders and written actions in lieu of meetings, provided, however, that except as otherwise required by law, holders of common stock as such shall not be entitled to vote on any amendment to the Company's Certificate of Incorporation that relates solely to the terms of one or more outstanding series of Preferred Stock if the holders of such affected series are entitled, either separately or together with the holders of one or more other such series, to vote thereon pursuant to the Company's Certificate of Incorporation or pursuant to Delaware General Corporation Law. There shall be no cumulative voting.

Dividends

The holders of shares of common stock are entitled to receive dividends, if and when declared by the Board of Directors. Cash dividends may not be declared or paid to the holders of common stock until paid on the preferred stock. As of December 31, 2017, no dividends have been declared or paid since the Company's inception.

Liquidation

After payment to the holders of shares of preferred stock of their liquidation preference, the holders of the common stock are entitled to share ratably in the Company's assets available for distribution to stockholders, in the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company or upon the occurrence of a Deemed Liquidation Event.

Reserve for future issuance

As of December 31, 2016, the Company had not reserved any shares of common stock for future issuance. As of December 31, 2017, the Company has reserved the following number of shares of common stock for future issuance upon the conversion of preferred stock, exercise of options or grant of equity awards:

	As of December 31, 2017
Redeemable convertible preferred stock, on an as-converted basis	15,870,559
Options issued and outstanding	195,668
Options available for future grants	1,670,341
Total	17,736,568

9. Stock-based Compensation

In 2017, the Company adopted the 2017 Stock Incentive Plan (the "Plan"). Under the Plan, shares of the Company's common stock have been reserved for the issuance of stock options to employees, directors, and consultants under terms and provisions established by the Board of Directors. A total of 537,914 shares were reserved for issuance under the Plan. Under the terms of the Plan, options may be granted at an exercise price not less than fair market value. The terms of options granted under the Plan may not exceed ten years. The Board shall determine the terms and conditions of a Restricted Stock Award, including the conditions for vesting and repurchase (or forfeiture) and the issue price, if any. On October 11, 2017, the Company increased the number of shares of common stock available for issuance under the Plan from 537,914 shares to 630,662 shares. On November 29, 2017, the Company increased the number of shares of common stock available for issuance under the Plan from 630,662 shares to 1,866,009 shares.

Stock-based Compensation Expense

Total stock-based compensation expense is recognized for stock options granted to employees and non-employees and has been reported in the Company's consolidated statements of operations as follows:

	Year Ended December 31, 2017	July 5, 2016 (inception) through December 31, 2016
	(In thousands)	
Research and development	$ 246	$ —
General and administrative	224	—
Total stock-based compensation expense	$ 470	$ —

Stock Options

The following table summarizes stock option activity under the Plan:

	Shares Available for Grant	Number of Options Outstanding	Weighted-Average Exercise Price per Option	Weighted-Average Remaining Contract Term	Aggregate Intrinsic Value
					(In thousands)
Outstanding, December 31, 2016	—	—	$ —		
Shares reserved for issuance	1,866,009				
Options granted(1)	(195,668)	195,668	4.49		
Outstanding, December 31, 2017	1,670,341	195,668	4.49	9.67	$ 1,699
Exercisable, December 31, 2017		—	—		
Vested and expected to vest, December 31, 2017		195,668	4.49	9.67	$ 1,699

(1) The Company granted 46,860 stock options to non-employees during the year ended December 31, 2017.

The aggregate intrinsic values of options outstanding, exercisable, vested and expected to vest were calculated as the difference between the exercise price of the options and the estimated fair value of the Company's common stock, as determined by the board of directors, as of December 31, 2017. No options were exercised, cancelled or forfeited during the year ended December 31, 2017.

During the year ended December 31, 2017, the Company granted options to employees to purchase an aggregate of 148,808 common shares with a weighted-average grant date fair value of $3.75. During the year ended December 31, 2017, the Company granted options to non-employees to purchase an aggregate of 46,860 common shares with a weighted-average grant date fair value of $0.67. On December 1, 2017, a non-employee became an employee of the Company. The expense related to options granted to employees and non-employees was $28,000 and $59,000, respectively, for the year ended December 31, 2017. There were no stock options granted to employees or non-employees during the period from July 5, 2016 (inception) to December 31, 2016.

As of December 31, 2017, the total unrecognized compensation expense related to unvested employee options was $0.7 million which the Company expects to recognize over an estimated weighted-average period of 3.78 years. As of December 31, 2017, the total unrecognized compensation expense related to unvested non-employee options was $0.3 million which the Company expects to recognize over an estimated weighted-average period of 3.45 years.

The fair value of stock options for employees and non-employees was estimated using a Black-Scholes option pricing model with the following assumptions:

	Year Ended December 31, 2017
Employees:	
Fair value of common stock	$0.79 - $9.33
Expected term (in years)	5.9-6.2
Expected volatility	74.4%-74.5%
Risk-free interest rate	1.9%-2.2%
Expected dividend yield	0.0%
Non-employees:	
Fair value of common stock	$0.79 - $1.00
Expected term (in years)	10.0
Expected volatility	74.6%-76.9%
Risk-free interest rate	2.3%
Expected dividend yield	0.0%

Fair Value of Common Stock: Given the absence of a public trading market, the Board of Directors considered numerous objective and subjective factors to determine the fair value of common stock at each grant date. These factors included, but were not limited to, (i) contemporaneous valuations of common stock performed by independent third-party specialists; (ii) the prices for preferred stock sold to outside investors; (iii) the rights, preferences and privileges of preferred stock relative to common stock; (iv) the lack of marketability of common stock; (v) developments in the business; and (vi) the likelihood of achieving a liquidity event, such as an initial public offering or a merger or acquisition of the Company, given prevailing market conditions.

Restricted Stock

On July 11, 2016, certain founding non-employee directors purchased 3,772,726 common shares that are subject to a repurchase right upon termination or cessation of services at the original purchase price of $0.0001 per share, or $483. Compensation expense of such unvested shares was remeasured at fair value until vested at each reporting date. On April 4, 2017, the non-employee directors became employees of the Company and as a result, compensation expense of the unvested shares was remeasured at fair value and fixed and is being recognized over the remaining vesting period. The repurchase right lapses as vesting occurs.

The summary of restricted stock activity and related information follows:

	Number of Restricted Shares Outstanding
Unvested shares — July 5, 2016 (inception)	—
Issued	3,772,726
Vested	(2,082,860)
Unvested shares — December 31, 2016	1,689,866
Vested	(593,417)
Unvested shares — December 31, 2017	1,096,449

The Company recognized $0.4 million and $0 of stock based compensation expense related to restricted shares during the year ended December 31, 2017 and the period from July 5, 2016 (inception) to December 31, 2016, respectively. As of December 31, 2017, there was $0.9 million of unrecognized stock-based compensation expense related to unvested restricted stock. This amount is expected to be recognized over a remaining weighted-average period of 2.53 years.

10. Income Taxes

Provision for Income Taxes

For the year ended December 31, 2017 and the period from July 5, 2016 (inception) to December 31, 2016, the Company did not record a current or deferred income tax expense. The Company's consolidated loss before income taxes consists solely of a domestic loss.

A reconciliation of income tax expense computed at the statutory federal income tax rate to income taxes as reflected in the consolidated financial statements is as follows:

	Year Ended December 31, 2017	July 5, 2016 (inception) through December 31, 2016
	(In thousands)	
Income tax expense (benefit) at federal statutory rate	$ (11,484)	$ —
State taxes	(1,011)	—
Tax credits	(222)	—
Stock-based compensation	140	—
Federal tax rate change	2,202	—
Change in fair value of tranche rights	5,065	—
Change in valuation allowance	5,310	—
Income tax expense	$ —	$ —
Effective tax rate	0.0%	0.0%

On December 22, 2017, the Tax Cuts and Jobs Act ("TCJA") was signed into United States law. The TCJA includes a number of changes to existing tax law, including, among other things, a permanent reduction in the federal corporate income tax rate from 34% to 21%, effective as of January 1, 2018, as well as limitation of the deduction for net operating losses to 80% of annual taxable income and elimination of net operating loss carrybacks, in each case, for losses arising in taxable years beginning after December 31, 2017 (though any such net operating losses may be carried forward indefinitely). The tax rate change resulted in (i) a reduction in the gross amount of our deferred tax assets as of December 31, 2017, without an impact on the net amount of our deferred tax assets, which are recorded with a full valuation allowance, and (ii) no income tax expense or benefit being recognized as of the enactment date of the TCJA.

Deferred Tax Assets and Liabilities

Deferred income taxes reflect the net tax effects of loss and credit carryforwards and temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Significant components of deferred income taxes were as follows as of December 31, 2017 and 2016:

	As of December 31,	
	2017	2016
	(In thousands)	
Deferred tax assets:		
Net operating losses	$ 3,953	—
Capitalized license	896	—
Research credits	269	—
Accruals	176	—
Stock-based compensation	16	—
Total gross deferred tax assets	5,310	—
Less valuation allowance	(5,310)	—
Total deferred tax assets	—	—
Deferred tax liabilities:		
Depreciation and Amortization	—	—
Total gross deferred tax liability	—	—
Net deferred tax assets	$ —	$ —

Realization of deferred tax assets is dependent upon future earnings, if any, the timing and amount of which are uncertain. Due to the lack of earnings history, the net deferred tax assets have been fully offset by a valuation allowance. A valuation allowance of $5.3 million has been recorded for the year ended December 31, 2017.

Net Operating Loss and Tax Credit Carryforwards

As of December 31, 2017 and 2016, the Company had net operating loss carryforwards for federal income tax purposes of approximately $14.5 million and $1,000, respectively which will begin to expire in 2036. As of December 31, 2017 and 2016, the Company had total state net operating loss carryforwards of approximately $14.4 million and $1,000, respectively which will begin to expire in 2036. Utilization of some of the federal and state net operating loss and credit carryforwards are subject to annual limitations due to the “change of ownership” provisions under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, and similar state provisions. The annual limitations may result in the expiration of net operating losses and credits before utilization. The Company has not performed an ownership change analysis.

As of December 31, 2017 and 2016, the Company had federal research credits of $0.2 million and $0, respectively which will begin to expire in 2037 and state research credits of $60,000 and $0, respectively which will begin to expire in 2032. These tax credits are subject to the same limitations discussed above.

Unrecognized Tax Benefits

The Company has incurred net operating losses since inception and has no significant unrecognized tax benefits. If in the future the Company recognizes uncertain tax positions, the Company’s effective tax rate will be reduced. Currently, the Company has a full valuation allowance against its net deferred tax asset which would impact the timing of the effective tax rate benefit should any of these uncertain tax positions be favorably settled in the future. Any adjustments to uncertain tax positions would result in an adjustment of net operating loss or tax credit carry forwards rather than resulting in a cash outlay. As of December 31, 2017, the Company had no unrecognized tax benefits and no accrued interest or penalties related to uncertain tax positions.

Income tax returns are filed in the U.S. and Massachusetts. The Company is not currently under examination. Due to net operating losses and research credit carryovers, all of the tax years remain open to examination.

11. Commitments and Contingences

Litigation

The Company is not a party to any litigation and does not have contingency reserves established for any litigation liabilities as of December 31, 2017.

12. Net Loss per Share

As described in Note 2, the Company computes basic and diluted earnings (losses) per share using a methodology that gives effect to the impact of outstanding participating securities (the "two-class" method). Basic net loss per share is calculated by dividing net loss by the weighted-average number of common shares outstanding during the period and excludes any dilutive effects of share-based awards. Diluted net loss per share is computed giving effect to all potential dilutive common shares, including common stock issuable upon exercise of stock options, convertible preferred stock, and unvested restricted common stock. As the Company had net losses for the year ended December 31, 2017 and the period from July 5, 2016 (inception) to December 31, 2016, there is no income allocation required under the two-class method or dilution attributed to weighted average shares outstanding in the calculation of diluted loss per share.

13. Related Party Transactions

Since the Company's incorporation in July 2016, the Company has engaged in transactions with related parties. The transactions were on terms comparable to terms that could have been obtained from unrelated third parties.

During the year ended December 31, 2017, the Company issued 1,886,363 shares of common stock and made payments to PureTech for certain founding services and cost reimbursements. PureTech is a founder of the Company and holds shares of common stock and preferred stock of the Company (See Note 7).

The Company is a party to an intellectual property license agreement with Novartis. In addition, NIBR is a preferred stock shareholder of the Company (See Note 6). During the year ended December 31, 2017, the Company made payments to Novartis for milestones achieved pursuant to the license agreement and for the purchases of materials for use in the Company's clinical trials.

Aggregate payments for the above related party transactions totaled $0.9 million for the year ended December 31, 2017. No payments were made to related parties during the period from July 5, 2016 (inception) to December 31, 2016.

14. Selected Quarterly Financial Data (Unaudited)

The following table contains quarterly financial information for 2017 and 2016. The Company believes that the following information reflects all normal recurring adjustments necessary for a fair statement of the information for the periods presented. The operating results for any quarter are not necessarily indicative of results for any future period.

	2017				
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter	Total
	(in thousands, except per share data)				
Total operating expenses	$ 3,357	$ 4,057	$ 3,945	$ 7,523	$ 18,882
Loss from operations	(3,357)	(4,057)	(3,945)	(7,523)	(18,882)
Net loss	(3,357)	(4,057)	(3,310)	(23,054)	(33,778)
Net loss applicable to common stockholders	(3,357)	(4,057)	(3,310)	(23,054)	(33,778)
Net loss per share applicable to common stockholders—basic and diluted	$ (1.20)	$ (0.94)	$ (0.75)	$ (5.11)	$ (8.42)

	2016				
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter	Total
	(in thousands, except per share data)				
Total operating expenses	$ —	$ 1	$ —	$ —	$ 1
Loss from operations	—	(1)	—	—	(1)
Net loss	—	(1)	—	—	(1)
Net loss applicable to common stockholders	—	(1)	—	—	(1)
Net loss per share applicable to common stockholders—basic and diluted	$ —	$ —	$ —	$ —	$ —

15. Subsequent Events

Reverse Stock Split

On January 12, 2018, the Company effected a one-for-1.2804 reverse stock split of its issued and outstanding shares of common stock and a proportional adjustment to the existing conversion ratios for each series of the Company's preferred stock. Accordingly, all common stock share and per share amounts and preferred stock conversion prices and ratios for all periods presented in the accompanying consolidated financial statements and notes thereto have been adjusted retroactively, where applicable, to reflect this reverse stock split and adjustment of the preferred stock conversion ratios.

In connection with the Company's IPO:

(i) The Company's board of directors adopted and the Company's stockholders approved the 2018 stock incentive plan ("2018 Plan"), which became effective immediately prior to the closing of the Company's initial public offering. The 2018 Plan provides for the grant of incentive stock options, nonstatutory stock options, restricted stock awards, restricted stock units, stock appreciation rights and other stock-based awards. The Company's employees, officers, directors, consultants and advisors are eligible to receive awards under the 2018 Plan. The number of shares of common stock that are reserved for issuance under the 2018 Plan are 2,200,260 shares. The 2018 Plan provides that the number of shares reserved and available for issuance under the plan will automatically increase each January 1, beginning on January 1, 2019, by 4% of the outstanding number of shares of the Company's common stock on the immediately preceding December 31 or such lesser number of shares as determined by the board of directors.

(ii) The Company's board of directors adopted and the Company's stockholders approved the 2018 employee stock purchase plan ("2018 ESPP"), which will become effective on a date determined by the Company's board of directors. Once effective, the 2018 ESPP will enable eligible employees to purchase shares of the Company's Common Stock at a discount. The number of shares of common stock that are reserved for issuance under the 2018 ESPP are 275,030 shares. The 2018 ESPP provides that the number of shares reserved and available for issuance under the plan will automatically increase each January 1, beginning on January 1, 2019 and each January 1 thereafter through January 1, 2028, by the least of (i) 1% of the outstanding number of shares of the Company's common stock on the immediately preceding December 31; (ii) 543,926 shares or (iii) or such number of shares as determined by the ESPP administrator.

RESTORBIO, INC.
SENIOR EXECUTIVE CASH INCENTIVE BONUS PLAN

1. Purpose

This Senior Executive Cash Incentive Bonus Plan (the "***Incentive Plan***") is intended to provide an incentive for superior work and to motivate eligible executives of resTORbio, Inc. (the "***Company***") and its subsidiaries toward even higher achievement and business results, to tie their goals and interests to those of the Company and its stockholders and to enable the Company to attract and retain highly qualified executives. The Incentive Plan is for the benefit of Covered Executives (as defined below).

2. Covered Executives

From time to time, the Compensation Committee of the Board of Directors of the Company (the "***Compensation Committee***") may select certain key executives (the "***Covered Executives***") to be eligible to receive bonuses hereunder. Participation in this Plan does not change the "at will" nature of a Covered Executive's employment with the Company.

3. Administration

The Compensation Committee shall have the sole discretion and authority to administer and interpret the Incentive Plan.

4. Bonus Determinations

(a) Corporate Performance Goals. A Covered Executive may receive a bonus payment under the Incentive Plan based upon the attainment of one or more performance objectives that are established by the Compensation Committee and relate to financial and operational metrics with respect to the Company or any of its subsidiaries (the "***Corporate Performance Goals***"), including the following: cash flow (including, but not limited to, operating cash flow and free cash flow); research and development, publication, clinical and/or regulatory milestones; earnings before interest, taxes, depreciation and amortization; net income (loss) (either before or after interest, taxes, depreciation and/or amortization); changes in the market price of the Company's common stock; economic value-added; acquisitions or strategic transactions, including licenses, collaborations, joint ventures or promotion arrangements; operating income (loss); return on capital, assets, equity, or investment; total stockholder returns; coverage decisions; productivity; expense efficiency; margins; operating efficiency; working capital; earnings (loss) per share of the Company's common stock; sales or market shares; number of prescriptions or prescribing physicians; revenue; corporate revenue; operating income and/or net annual recurring revenue, any of which may be (A) measured in absolute terms or compared to any incremental increase, (B) measured in terms of growth, (C) compared to another company or companies or to results of a peer group, (D) measured against the market as a whole and/or as compared to applicable market indices and/or (E) measured on a pre-tax or post-tax basis (if applicable). Further, any Corporate Performance Goals may be used to measure the performance of the Company as a whole or a business unit or other segment of the

Company, or one or more product lines or specific markets. The Corporate Performance Goals may differ from Covered Executive to Covered Executive.

(b) Calculation of Corporate Performance Goals. At the beginning of each applicable performance period, the Compensation Committee will determine whether any significant element(s) will be included in or excluded from the calculation of any Corporate Performance Goal with respect to any Covered Executive. In all other respects, Corporate Performance Goals will be calculated in accordance with the Company's financial statements, generally accepted accounting principles, or under a methodology established by the Compensation Committee at the beginning of the performance period and which is consistently applied with respect to a Corporate Performance Goal in the relevant performance period.

(c) Target; Minimum; Maximum. Each Corporate Performance Goal shall have a "target" (100 percent attainment of the Corporate Performance Goal) and may also have a "minimum" hurdle and/or a "maximum" amount.

(d) Bonus Requirements; Individual Goals. Except as otherwise set forth in this Section 4(d): (i) any bonuses paid to Covered Executives under the Incentive Plan shall be based upon objectively determinable bonus formulas that tie such bonuses to one or more performance targets relating to the Corporate Performance Goals, (ii) bonus formulas for Covered Executives shall be adopted in each performance period by the Compensation Committee and communicated to each Covered Executive at the beginning of each performance period and (iii) no bonuses shall be paid to Covered Executives unless and until the Compensation Committee makes a determination with respect to the attainment of the performance targets relating to the Corporate Performance Goals. Notwithstanding the foregoing, the Compensation Committee may adjust bonuses payable under the Incentive Plan based on achievement of one or more individual performance objectives or pay bonuses (including, without limitation, discretionary bonuses) to Covered Executives under the Incentive Plan based on individual performance goals and/or upon such other terms and conditions as the Compensation Committee may in its discretion determine.

(e) Individual Target Bonuses. The Compensation Committee shall establish a target bonus opportunity for each Covered Executive for each performance period. For each Covered Executive, the Compensation Committee shall have the authority to apportion the target award so that a portion of the target award shall be tied to attainment of Corporate Performance Goals and a portion of the target award shall be tied to attainment of individual performance objectives.

(f) Employment Requirement. Subject to any additional terms contained in a written agreement between the Covered Executive and the Company, the payment of a bonus to a Covered Executive with respect to a performance period shall be conditioned upon the Covered Executive's employment by the Company on the bonus payment date. If a Covered Executive was not employed for an entire performance period, the Compensation Committee may pro rate the bonus based on the number of days employed during such period.

5. Timing of Payment

(a) With respect to Corporate Performance Goals established and measured on a basis more frequently than annually (e.g., quarterly or semi-annually), the Corporate Performance

Goals will be measured at the end of each performance period after the Company's financial reports with respect to such period(s) have been published. If the Corporate Performance Goals and/or individual goals for such period are met, payments will be made as soon as practicable following the end of such period, but not later than 74 days after the end of the fiscal year in which such performance period ends.

(b) With respect to Corporate Performance Goals established and measured on an annual or multi-year basis, Corporate Performance Goals will be measured as of the end of each such performance period (e.g., the end of each fiscal year) after the Company's financial reports with respect to such period(s) have been published. If the Corporate Performance Goals and/or individual goals for any such period are met, bonus payments will be made as soon as practicable, but not later than 74 days, after the end of the relevant fiscal year.

(c) For the avoidance of doubt, bonuses earned at any time in a fiscal year must be paid no later than 74 days after the last day of such fiscal year.

6. Amendment and Termination

The Company reserves the right to amend or terminate the Incentive Plan at any time in its sole discretion.

Exhibit 21.1

SUBSIDIARIES

Subsidiary	Jurisdiction of Incorporation
resTORbio Securities Corp.	Massachusetts

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the registration statement (No. 333-222746) on Form S-8 of resTORbio, Inc. of our report dated March 29, 2018, with respect to the consolidated balance sheets of resTORbio, Inc. as of December 31, 2017 and 2016, and the related consolidated statements of operations, convertible redeemable preferred stock and stockholders (deficit) equity, and cash flows for the year ended December 31, 2017 and the period from July 5, 2016 (inception) through December 31, 2016, and the related notes (collectively, the "consolidated financial statements"), which report appears in the December 31, 2017 annual report on Form 10-K of resTORbio, Inc.

/s/ KPMG LLP

Boston, Massachusetts
March 29, 2018

Exhibit 31.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER PURSUANT TO RULE 13a-14(a) / RULE 15d-14(a) OF THE SECURITIES EXCHANGE ACT OF 1934, AS AMENDED

I, Chen Schor, certify that:

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

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

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

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

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

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

   c) (Paragraph omitted pursuant to SEC Release Nos. 33-8238/34-47986 and 33-8392/34-49313); and

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

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

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

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

/s/ Chen Schor

Chen Schor
President and Chief Executive Officer
(Principal Executive Officer)

Dated: March 29, 2018

Exhibit 31.2

CERTIFICATION OF PRINCIPAL FINANCIAL OFFICER PURSUANT TO RULE 13a-14(a) / RULE 15d-14(a) OF THE SECURITIES EXCHANGE ACT OF 1934, AS AMENDED

I, John J. McCabe, certify that:

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

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

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

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

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

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

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

   d) (Paragraph omitted pursuant to SEC Release Nos. 33-8238/34-47986 and 33-8392/34-49313); and

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

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

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

/s/ John J. McCabe

John J. McCabe
Vice President, Finance
(Principal Financial Officer)

Dated: March 29, 2018

Exhibit 32.1

CERTIFICATIONS OF PRINCIPAL EXECUTIVE OFFICER AND PRINCIPAL FINANCIAL OFFICER PURSUANT TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of resTORbio, Inc. (the "Company") for the fiscal year ended December 31, 2017 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), the undersigned hereby certify, pursuant to 18 U.S.C. Section 1350, that, to the best of their knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

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

/s/ Chen Schor

Chen Schor
President and Chief Executive Officer
(Principal Executive Officer)

Dated: March 29, 2018

/s/ John J. McCabe

John J. McCabe
Vice President, Finance
(Principal Financial Officer)

Dated: March 29, 2018