Aimmune Therapeutics, Inc.
Form 10-K
March 15, 2017

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, 2016

OR

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

Commission File Number 001--37519

AIMMUNE THERAPEUTICS, INC.

(Exact name of Registrant as specified in its Charter)

Delaware	45-2748244
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

8000 Marina Blvd Suite #300

Brisbane, CA 94005

(Address of principal executive offices)

(650) 614-5220

(Registrant's telephone number, including area code)

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

Title of each class	Name of exchange on which registered
Common Stock, par value $0.0001 per share	The 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 (§232.405 of this chapter) 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 (§229.405) 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, or a smaller reporting company. See the definition of "large accelerated filer", "accelerated filer", and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer		Accelerated filer
Non-accelerated filer	(Do not check if a small reporting company)	Small reporting company

Indicate by check mark whether the Registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES NO

The aggregate market value of voting common equity held by non-affiliates of the Registrant was $365,306,236 as of June 30, 2016.

As of March 10, 2017, there were 50,249,376 shares of the Registrant's common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's Definitive Proxy Statement relating to the 2017 Annual Meeting of Shareholders, scheduled to be held on May 25, 2017, are incorporated by reference into Part III of this Annual Report on Form 10-K to the extent stated herein. The Definitive Proxy Statement will be filed within 120 days of the Registrant's fiscal year ended December 31, 2016.

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PART I

Item 1. Business.

Overview

We are a clinical-stage biopharmaceutical company advancing a new therapeutic approach, including the development of proprietary product candidates, for the treatment of peanut and other food allergies. It is estimated that over 30 million people in the United States and Europe have a food allergy, with peanut allergy being the most prevalent and most commonly associated with severe outcomes and life-threatening events. There are currently no approved medical therapies to cure food allergies or prevent their symptoms. Patients with food allergies are typically counseled to practice strict dietary avoidance. When accidental exposure to food allergens invokes a serious allergic reaction, rescue therapies, such as antihistamines or injectable epinephrine, are the only recourse available. Our therapeutic approach, which we refer to as Characterized Oral Desensitization ImmunoTherapy, or CODIT™, is designed to desensitize patients to food allergens and thereby reduce the risk of having an allergic reaction upon accidental exposure, or reduce symptom severity should an allergic reaction occur. CODIT is intended to reduce meaningfully the burden and anxiety experienced by food-allergic patients and their families.

Our lead CODIT product candidate, AR101, is an investigational biologic for the treatment of patients with peanut allergy, which affects approximately three million patients in the United States and three million patients in Europe. AR101 has received Fast Track and Breakthrough Therapy Designations for the treatment of patients 4-17 years from the United States Food and Drug Administration, or FDA. Our initial target patient population is in children and adolescents in the 4-17 age group, which we estimate will reach approximately 1.6 million patients in the United States alone by 2018. We have completed a double-blind placebo-controlled Phase 2 trial of AR101 in 55 patients ages 4-21 years, have analyzed longer-term safety and efficacy data from our ongoing open-label Phase 2 trial and have received feedback from regulatory authorities, including the FDA and the European Medicines Agency, or EMA, providing guidance on our Phase 3 program. In late 2015, we initiated a Phase 3 registration trial of AR101 in the United States, Canada and Europe, which we refer to as the PALISADE (Peanut Allergy Oral Immunotherapy Study of AR101 for Desensitization in Children and Adults) trial. We completed global enrollment of 554 patients ages 4-49 in November 2016 and anticipate completing the PALISADE trial around year-end 2017. We have begun to enroll eligible patients who have completed PALISADE into a related open-label Phase 3 roll-over trial, which we refer to as the ARC004 trial. We expect to begin enrolling a real-world experience trial of AR101 in the United States and Canada in patients ages 4-17 in the second quarter of 2017, which we refer to as the RAMSES (Real-World AR101 Market-Supporting Experience Study in Peanut Allergic Children Ages 4-17 Years) trial. In addition, we expect to initiate a European trial in the middle of 2017 designed with a higher efficacy bar in the same age group, which we refer to as the ARTEMIS (AR101 Trial in Europe Measuring oral Immunotherapy Success) trial. Based on discussions with the FDA in the beginning of 2017, we anticipate that the safety database for a Biologics License Application, or BLA, will need to include data from at least 600 patients ages 4-17 treated with AR101 at the target maintenance dose of 300 mg per day. We expect to meet this requirement with patients from the PALISADE, ARC004 and RAMSES trials. In Europe, we expect that data from the PALISADE, ARC004 and ARTEMIS trials will form the basis for a Marketing Authorization Application, or MAA, filing with the European Medicines Agency, or EMA. We expect to have topline data from our PALISADE trial around year-end 2017 and intend to file a BLA in the United States and an MAA in the European Union in late 2018.

In November 2016, we entered into a two-year strategic collaboration with an affiliate of Nestle Health Science US Holdings, Inc. for the advancement of food allergy therapeutics and issued and sold to Nestle Health Science US Holdings, Inc. (together with its affiliate, Nestle Health Science) $145 million of shares of our common stock in a

private placement. We maintain worldwide commercial rights to all of our product candidates, including AR101 and, if approved, currently intend to commercialize in the United States and Europe with our own specialty sales force calling on allergists in the United States and allergy-focused clinicians in major European markets.

Our Strategy

Our goal is to build a biopharmaceutical company that develops and commercializes proprietary therapies to improve the lives of food-allergic patients and their families. We intend to achieve this goal by pursuing the following key strategic objectives:

- Complete development and obtain approval of AR101 in the United States and Europe for the treatment of peanut allergy: We expect to have topline data from our Phase 3 PALISADE trial of AR101 around year-end 2017, and intend to file a BLA in the United States and a MAA in the European Union in late 2018.
- Commercialize AR101 in the United States and Europe through our own specialty sales force: We own worldwide commercial rights to our product candidates. If AR101 is approved for the treatment of peanut allergy, we intend to commercialize it by developing a specialty sales force targeting a subset of the approximately 5,000 practicing allergists in the United States as well as allergy-focused clinicians in the major European markets. We anticipate that this sales force could also support the commercialization of additional CODIT product candidates, if approved

- Leverage the CODIT system to develop additional proprietary product candidates for the treatment of food allergies: Leveraging the expertise we have gained developing AR101, we have and expect to continue to conduct activities to support the filing of an Investigational New Drug, or IND, application for a product candidate for the treatment of egg allergy. We have also initiated pre-clinical development of a product candidate for the treatment of tree nut allergy.

AR101 Program Overview

Peanut allergy is a life-threatening disease with no approved medical treatment options. Based on a 2014 study published in the Journal of Allergy and Clinical Immunology, 40% to 50% of the people with peanut allergy in the United States are sensitive to an exposure of 100 mg or less of peanut protein, the equivalent of less than half of a peanut kernel (one peanut kernel typically contains approximately 250 mg to 300 mg of peanut protein). In addition, people with peanut allergy are often sensitive to as little as 10 mg of peanut protein. Strict dietary avoidance is hard to achieve and accidental exposure to food allergens is common, resulting in approximately 200,000 emergency room visits per year in the United States. The burden and anxiety for patients and their families is significant and a highly motivating force in seeking out therapy. There is a particularly high unmet need in young children who spend a significant portion of their day away at school where parental control is diminished and in adolescents who face peer pressure from their friends and classmates and may begin to engage in risk-taking behaviors.

Allergists have long used immunotherapy approaches to treat successfully patients with environmental allergies, and academic research supports the potential for extending immunotherapy approaches to treating patients with food allergy. Published studies have shown oral immunotherapy (OIT) to be a potentially promising approach to desensitizing patients with peanut, milk, egg, and other food allergies. This approach involves gradual introduction of increasing amounts of food allergen by the oral route to reduce the immune response to that allergen, referred to as the build-up or up-dosing phase, and then daily ingestion of the target dose of allergen to maintain the achieved level of desensitization, referred to as the maintenance phase. Historically, OIT has been practiced by a small number of allergists using their own “home-brew” allergen formulations and desensitization protocols; however, no OIT-based products have been approved for the treatment of food allergies to date thereby limiting the widespread adoption of this approach. With CODIT, we believe that we are the first company to undertake systematic and rigorous development of an OIT-based therapeutic approach to treat food allergies. We believe that AR101 has the potential to fulfill the need for a consistent and scalable OIT-based approach to peanut allergy.

In 2015, we completed a double-blind placebo-controlled Phase 2 trial in 55 peanut-allergic patients ages 4-17, which we refer to as the ARC001 trial. Results were reported at the 2015 annual meeting of the European Academy of Allergy and Clinical Immunology (EAACI). In the ARC001 trial, we measured subjects’ levels of sensitivity to peanut protein using the double-blind placebo-controlled food challenge (DBPCFC). A DBPCFC is generally considered the “gold standard” method of measuring a patient’s sensitivity to peanuts or other foods. During the DBPCFC, subjects consume increasing amounts of a peanut protein until either the test is naturally concluded or until a dose-limiting reaction, typically moderate or severe, occurs at which point the subject is not permitted to proceed to the next step in the challenge and the test is halted. The primary efficacy endpoint of ARC001 was the percentage of patients up-dosed for approximately six months with AR101 who could tolerate a cumulative of 443 mg of peanut protein, or about one to one and a half peanuts, a level which we believe is in excess of that typically encountered upon accidental exposure. The maximum tolerated amount of peanut protein refers to the total amount of peanut protein that could be consumed during the DBPCFC with the subject experiencing no more than mild symptoms. In the group of 29 patients that were treated with AR101, six patients discontinued the trial early during up-dosing due to gastrointestinal symptoms, which resolved within one to three weeks upon cessation of therapy in all cases, a finding consistent with previous literature reports of gastrointestinal side effects associated with OIT. As depicted in the graph below, results of the six-month DBPCFC showed on an intent-to-treat basis that 79% of patients (23 of 29) in the AR101-treated group were able to tolerate a cumulative amount of at least 443 mg of peanut protein versus 19% (5 of 26) of placebo patients, resulting in a p-value of <0.0001. One hundred percent (100%) of patients who completed up-dosing in the AR101-treated group were able to tolerate a cumulative amount of at least 443 mg of peanut protein. Treatment with AR101 also reduced symptom severity during the DBPCFC compared to placebo. Adherence to the dosing schedule, which refers

to the percentage of full or partial doses taken at home, was 95%.

Upon completion of the ARC001 trial, we offered patients the opportunity to participate in the open-label Phase 2 study, which we refer to as the ARC002 trial, and either continue to receive AR101 maintenance therapy at a low daily dose of 300 mg per day of AR101 if they had been in the AR101-treated group in ARC001, or cross over to undergo up-dosing with AR101 and then continue on maintenance therapy if they had been in the placebo group in ARC001. Approximately 96% (47 of 49) of patients who completed the ARC001 trial elected to participate in the ARC002 trial. Preliminary results were reported at the 2016 annual meeting of The American Academy of Asthma, Allergy & Immunology (AAAAI). A total of 40 patients completed nine months of AR101 therapy (six months of up-dosing and three months of maintenance dosing with 300 mg of AR101 per day) at which point a DBPCFC was conducted and showed that 100%, 90%, and 60% of patients tolerated cumulative amounts of peanut protein of 443 mg, 1,043 mg, and 2,043 mg, respectively (corresponding to 85%, 77%, and 51% on an intent-to-treat basis). The highest challenge level was the equivalent of seven or eight peanuts. In June 2016, we reported results from the extended maintenance portion of the ARC002 trial at the EAACI annual meeting.

We offered patients who completed the nine-month DBPCFC the opportunity to continue on extended maintenance therapy with AR101. All of the 40 patients who complete the initial portion of the ARC002 trial elected to continue on extended maintenance therapy with AR101. Of these, 11 elected to remain on CODIT maintenance therapy of 300 mg of AR101 per day, and 29 chose to attempt up-dosing to high-dose maintenance therapy. With data for treatment with AR101 for at least a year in all of the patients, we reported that most side effects associated with AR101 are typically mild, manageable gastrointestinal side effects that happen early in up-dosing and that the rate of related adverse events decreases substantially during extended maintenance, particularly with low-dose CODIT maintenance of 300 mg of AR101 per day. In this study, peanut taste with the CODIT maintenance dose was observed to be minimal, which we believe is an important consideration in maintaining compliance, especially for those patients who have a strong aversion to the taste of peanut.

In December 2015, we initiated the Phase 3 PALISADE trial, which was designed to enroll approximately 500 peanut-allergic patients 4-55 years of age. We completed enrollment in the United States and Canada in September 2016 and announced plans to initiate the RAMSES trial in the United States and Canada, which does not require a DBPCFC and therefore reflects our expectations for the real world experience with AR101 where a DBPCFC is not required for diagnosis of peanut allergy. We subsequently announced completion of European enrollment in November 2016 and our plans to initiate the ARTEMIS trial in children and adolescents in Europe, which is designed to evaluate a higher efficacy bar of tolerating a cumulative amount of 2,043 mg of peanut protein after nine months of AR101 therapy.

In the first quarter of 2017, the FDA provided feedback on the RAMSES study protocol and overall Phase 3 program for AR101. As a result, we are now going to conduct the primary efficacy analysis for the PALISADE trial in the 4-17 age group in which we enrolled 498 patients, or 90% of the total number of patients enrolled in the PALISADE trial. This age group aligns with the patient population enrolled in our Phase 2 trials for which AR101 received Breakthrough Therapy Designation based on the encouraging results observed in those trials. We will conduct separate analyses on the 56 adults enrolled in PALISADE. The FDA provided additional clarification related to using the most clinically meaningful nomenclature when reporting the results of the DBPCFC. As a result, we will report the single highest tolerated dose in the food challenge as an appropriate and clinically meaningful measure. We will therefore report the primary efficacy endpoint in PALISADE as the single highest tolerated dose of 600 mg, which corresponds to a cumulative amount of 1,043 mg peanut protein. Based on discussions with the FDA, we anticipate that the safety database for a BLA will need to include data from at least 600 patients ages 4-17 treated with AR101 at the target maintenance dose of 300 mg per day. We expect to fulfill that requirement with patients from PALISADE, ARC004 and RAMSES. In Europe, we

expect data from PALISADE, ARC004 and ARTEMIS will form the basis for the MAA filing. We expect to have topline data from our PALISADE trial around year-end 2017 and intend to file a BLA in the United States and an MAA in the European Union in late 2018.

We have worldwide development and commercialization rights to AR101. Subject to regulatory approval, we intend to commercialize AR101 in the United States and Europe by developing a specialty sales force targeting a subset of the approximately 5,000 practicing allergists in the United States as well as allergy-focused clinicians in major European markets.

Food Allergy Overview

Food Allergies are a Significant and Growing Health Problem

Food allergies are a significant and growing health problem in the United States, Europe and throughout the developed world. It is estimated that over 30 million people in the United States and Europe have a food allergy, and one in 13 children are affected in the United States. According to a study published in JAMA Pediatrics in 2013, the economic cost of food allergies in the United States is estimated to equal approximately $25 billion per year, of which approximately $4 billion is associated with direct medical expenses. Food allergies are a particularly urgent issue for children and adolescents because of the greater prevalence of food allergies in those age groups and because of the increased risk of accidental exposures leading to a serious allergic reaction. A large scale study conducted in 2011 concluded that approximately 8% of children and adolescents in the United States have a food allergy and that approximately 39% of that group had a history of at least one severe allergic reaction. We estimate that over 50% of patients with peanut allergy experience a severe allergic reaction each year.

Peanut is the most common type of food allergy. Among children with food allergies in the United States, approximately 25% are allergic to peanuts, with other common food allergies being milk (21%), shellfish (17%), tree nut (13%) and egg (10%). We estimate that there are approximately three million people in the United States and three million people in Europe with peanut allergy, including over three million children. The prevalence of peanut allergy in children in the United States is estimated to have increased at a constant annual growth rate of approximately 10% between 1997 and 2008, and experts believe it has continued to rise since 2008.

Risks Associated with Allergic Reactions

Allergic reactions to food are painful, frightening and potentially deadly. Symptoms of an allergic reaction include hives, swelling, vomiting, abdominal pain, wheezing, breathlessness, and lowered blood pressure. Severe and potentially life-threatening reactions are referred to as anaphylaxis and such reactions require urgent medical attention and often result in treatment at hospital emergency departments. Food-related allergic reactions are estimated to result in approximately 200,000 emergency room visits and over 10,000 hospital admissions each year in the United States.

Allergic reactions, including severe allergic reactions, can be triggered by exposure to minute quantities of the relevant food allergen. For example, of the over two million people with peanut allergy in the United States, 40% to 50% are sensitive to an exposure of 100 mg or less of peanut protein, the equivalent of less than half of a peanut kernel (one peanut kernel typically contains approximately 250 mg to 300 mg of peanut protein). In addition, people with peanut allergy are often sensitive to as little as 10 mg of peanut protein, the equivalent of approximately 1/25th of a peanut kernel. As a result, accidental exposure arising from contamination of a food source or the inaccurate or confusing labeling of food products occurs regularly and can result in severe allergic reactions.

Causes of Allergic Reactions

Food allergies occur when the immune system responds to a harmless food as if it were a threat. The human gastrointestinal tract contains immune cells whose purpose is to identify and mount a response against proteins

deemed to be foreign and unsafe. These cells come into contact with a large amount and variety of food proteins. In a non-allergic person, a tolerance for food proteins develops early in life, and the immune cells do not mount a response when food proteins are detected. In contrast, in an allergic patient, the immune system is sensitized to one or more food proteins, or allergens. As a result of this sensitization, the immune system produces antibodies, known as IgE antibodies, which are directed against a particular allergen, such as a specific peanut protein. The IgE antibodies link with mast cells and basophils, which are other immune cells. When an IgE antibody linked to these immune cells encounters the allergen it is directed against, the immune cells are activated and release histamine and other inflammatory mediators into the blood. These mediators then provoke the symptoms of an allergic reaction.

The development and progression of food allergies is highly variable. It is unknown why some people develop food allergies while others do not. For certain types of allergies, such as milk and egg, patients may outgrow their allergies, but for others, such as peanuts, tree nuts and shellfish, most patients remain allergic for life. In addition, a person's sensitivity appears to vary over time based on a range of factors. It is not unusual for a person's first allergic reaction to be mild and their second allergic reaction to be severe or life-threatening.

Challenges in the Current Treatment and Management of Food Allergies

There are currently no approved medical therapies to cure food allergies or prevent their symptoms. The most common practices are strict avoidance of food allergens and emergency treatment of allergy symptoms in the event of an accidental exposure. These options have substantial limitations, and the burdens of practicing avoidance and stress caused by the limited availability of effective treatment options for accidental exposure can have a substantial negative impact on the quality of life of food-allergic patients and their families. For example, food-allergic patients and their caregivers often have difficulties managing their social and day-to-day lives, and live with an ongoing fear of accidental exposure and anaphylaxis. One study found that children with peanut allergy reported a poorer quality of life than children with insulin-dependent diabetes mellitus. A separate study found that the parents of peanut-allergic children reported more disruption in their family's lives than the parents of children with rheumatological disease.

Limitations of Practicing Avoidance of Food Allergens

Successfully practicing avoidance can be very difficult and requires careful reading of food labels, care in the storage and preparation of foods, awareness of product recalls for mislabeling and contamination, and oftentimes avoidance of cuisines where the food allergen is known to be common. In addition, activities such as attending a sporting event, traveling by airplane or visiting public spaces become difficult and stressful for food-allergic patients and their families. Practicing avoidance can be particularly difficult on food-allergic children as parents often attempt to prevent accidental exposures by limiting their child's participation in everyday activities, including social activities, eating outside the home and sometimes even choosing to home school their child because such food-allergic children may not have the awareness or self-regulation skills to practice avoidance by themselves. As children move into adolescence and young adulthood, decreased parental supervision and increased societal pressures often complicate the practice of avoidance.

Limitations of Emergency and Symptomatic Treatments

Due to a lack of approved symptomatic or disease-modifying food allergy treatments, food-allergic patients typically must carry rescue medication to treat severe and possibly life-threatening allergic reactions. The most widely used treatment is epinephrine (also known as adrenaline), which is administered using an auto-injector, such as an EpiPen. Epinephrine blunts certain symptoms of the allergic reaction by increasing heart rate and blood pressure and dilating airways, but it does not treat the allergic reaction itself. While epinephrine is useful as a rescue medication, it is not always administered properly or quickly enough and may not be sufficient to counteract the effects of the allergic reaction.

Limitations of Current Desensitization Treatments

Emergency and symptomatic remedies are reactive treatments and often ineffective in the chronic management of food allergies. The most commonly practiced proactive therapy for food and other allergies is desensitization therapy. Desensitization therapy consists of repeated administrations of increasing quantities of an allergen to an allergic patient in order to decrease the immune response to that allergen. The most common form of desensitization therapy is subcutaneous injections for patients with environmental allergies. While desensitization therapy has had significant success in the treatment of environmental allergies, it has been less successful in the treatment of food allergies. Four different desensitization therapy approaches to food allergies have been researched:

- Subcutaneous Injections: Involves the subcutaneous injection of the food allergen. This approach has been shown to induce desensitization in some patients but has had an unacceptably high incidence of adverse events and research on this approach has largely been abandoned.
- Sublingual Immunotherapy: Involves the administration of increasing amounts of food extract under a patient's tongue. This approach has been shown to be safe, but it appears to induce only a modest degree of desensitization.
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- Epicutaneous Desensitization: Involves the use of a patch that causes allergens to be absorbed by the skin. Clinical trials are ongoing to explore the potential viability of this approach.
- Oral Immunotherapy: Involves the administration of increasing doses of a food-based product on a daily basis over a period of months. This approach has the potential to produce a high degree of desensitization but adoption has been hampered by lack of standardization for products and protocols.

We believe the most effective form of desensitization therapy is oral immunotherapy, or OIT.

Immunology of Oral Desensitization

Oral desensitization works by gradually shifting the balance of the immune system to dampen the allergic response in the case of accidental exposure.

The initial step in an immune response is the presentation of an allergenic protein by an antigen presenting cell, such as a dendritic cell, and subsequent recognition of the allergenic protein by T-cells. A subset of T-cells, known as Th2 cells, upon binding to an antigen secrete a set of pro-inflammatory proteins called cytokines, such as IL-4, IL-5 and IL-13, which are important in cellular activation and signaling. Secretion of this group of cytokines promotes B-cell maturation and production of IgE antibodies. These IgE antibodies cross-link at the surface of the mast cells by binding with the antigen, which results in the mast cells releasing histamines, proteases and other chemical mediators of inflammation, all of which elicit symptoms of an allergic reaction.

In oral desensitization, the step-wise increasing of doses of an allergen, starting with very low levels of such allergen that are generally insufficient to trigger a large IgE-mediated allergic reaction, has been shown over time to induce regulatory T-cells. These regulatory T-cells dampen the Th2 immune response. At the same time, the increasing levels of allergen exposure induce B-cells to produce IgG4 antibodies, which compete with IgE antibodies to bind with the allergen, thereby decreasing allergen-induced mast cell degranulation. Ultimately, these immunomodulatory T-cell and B-cell responses result in a decreased clinical response to allergen exposure.

Oral Desensitization in Practice

In an OIT treatment regimen, the initial administration of a particular dose of the food allergen will typically be provided in an allergist's office and the subsequent administrations will be done at home. The highest level of dosing administration will vary depending on the patient and the protocol, but generally the goal is to achieve desensitization to a level of food allergen greater than the amount a patient might be exposed to in an accidental exposure. Once the highest dosing level is attained, the patient will continue to be administered a maintenance dose on a regular basis. Over time, this regular administration has been shown to result in the patient being able to tolerate an amount of food substantially greater than the maintenance dose.

Numerous clinical trials at leading academic research centers have shown that OIT can desensitize patients to a range of food allergies, including peanut, egg and milk. While OIT generally does not cure a patient of his or her allergy, it can provide protection from food allergens at a level that exceeds the amount typically encountered in an accidental exposure. For many patients, this protection meaningfully decreases their stress and anxiety and enables them to lead a more normal life.

While OIT has been shown to be effective, it has not been widely adopted and is currently available only from a limited number of academic research centers and specialized allergy clinics. These institutions have access to compounding pharmacies to produce the doses of food-based product necessary for the therapy and also have the resources to provide the required patient support. However, because no OIT protocol or product has been validated in a large-scale clinical trial or approved by the FDA, the treatment regimen and food source used in OIT treatment is determined by the allergist based on their experience and review of the scientific literature, which can lead to varying results. While studies have shown that most patients tolerate OIT well, the incidence of severe adverse events associated with OIT treatment has historically been high enough to raise concerns in the medical community that it is not safe enough to be a standard part of an allergist's practice. We believe these safety concerns along with complexity and lack of standardization have limited the adoption of OIT by community-based allergists.

Our Solution

Our CODIT approach for the treatment of food allergies leverages and improves upon the extensive independent scientific research supporting OIT. Based on our clinical development to date, including our Phase 2 studies of our lead CODIT product candidate, AR101, we believe that our CODIT approach has the potential to be widely adopted by allergists and to appeal to patients and parents as a result of the following key attributes:

- Standardized Products: Our proprietary biologic product candidates are derived from natural food products and are designed to contain precisely defined dosages of well-characterized food proteins so that each dosage is consistent

for total protein and relative allergen content. In addition, we expect each of our product candidates, if approved, to be provided to patients as a convenient, orally administered, once daily therapy.

- Safe and Well-Defined Treatment Regimens: We intend to demonstrate the safety and efficacy of each CODIT product candidate in large scale, well-controlled clinical trials. In addition, we expect each CODIT product candidate to feature clearly defined clinical protocols with gradual up-dosing and practical maintenance dosing regimens designed to enhance safety, tolerability and efficacy.

- Clinically Meaningful Desensitization: We expect each approved CODIT product candidate to provide patients with protection from food allergens at a level that exceeds the amount typically encountered in an accidental exposure, to impart real world safety.
- Compatibility with Clinical Practice: We expect our protocols for each CODIT product candidate to be similar to treatment regimens currently utilized by allergists for non-food allergies.

- Tailored Support Services: We intend to provide physician education, patient guidance and other support services to facilitate the administration of each approved CODIT product candidate.
- Regulatory Approval: We believe regulatory approval of our CODIT product candidates, if obtained, will validate the extensive existing scientific research supporting oral desensitization and could lead to widespread adoption of CODIT.

We believe our CODIT approach and product candidates, if approved, have the potential to reduce the dangers posed to food-allergic patients, such as accidental exposures resulting in anaphylactic reactions, emergency room visits or hospitalization. We expect that this potential protection from accidental exposures will reduce the stress and anxiety of patients and their families and enable patients to live more normal lives.

AR101 for Peanut Allergy

Overview

We are developing our lead CODIT product candidate, AR101, for the treatment of peanut allergy. Our initial target patient population is children and adolescents ages 4-17 years. AR101 is intended to desensitize patients to a level of peanut protein that substantially exceeds the amount typically encountered in an accidental exposure. Patients successfully treated with AR101 will still need to avoid the consumption of peanuts and foods containing peanuts, but we believe that protection against potential allergic reactions to accidental exposure will significantly improve the lives of food-allergic patients and their families.

We believe AR101, if approved, will provide allergists with a safe and practical means of providing oral desensitization treatment to their patients with peanut allergy. AR101 is designed to be taken orally once daily after having been mixed with a common age-appropriate food. As with OIT, patients would start with a very low dose of AR101 and gradually increase their dose over time. The initial assessment of patients and each initial increase in dosage would occur at an allergist's office. Based on our existing clinical data, we anticipate it will take patients approximately six months to reach a daily dose level of 300 mg of peanut protein. Patients would then continue on a daily 300 mg maintenance dose. Based on independent scientific research, we anticipate that with continued maintenance dosing, patients' level of desensitization will increase over time. In order to maintain desensitization, patients would need to continue to take a daily 300 mg maintenance dose; however, based on experience with OIT, we do not believe that the occasional failure to take a maintenance dose will significantly affect desensitization.

Our up-dosing and maintenance dosing regimens are set forth below:

For patients in the up-dosing phase of the AR101 treatment regimen, AR101 would be provided in a series of color coded pharmaceutical grade capsules of various dose levels. These capsules can be easily opened and emptied, with the contents then mixed with food. For patients who have reached the 300 mg maintenance dose level, AR101 would be provided in an easy to open-and-empty sachet. We are in the process of evaluating additional delivery forms for AR101 for the maintenance phase.

AR101 Product Characteristics

We believe the following characteristics of AR101 could enable it, if approved, to achieve widespread market acceptance and distinguish it from existing treatments and potentially competing products in development:

- Proprietary Biologic Product: Our proprietary formulation is a complex mixture of a full range of naturally occurring proteins and pharmaceutical-grade ingredients that we developed to enable the convenient dosing of consistent amounts of peanut protein with well-defined relative concentrations of peanut specific allergens.
- Clinically Meaningful and Reliable Desensitization: Based on the results of our Phase 2 studies of AR101, we believe that patients who successfully complete the AR101 up-dosing regimen will be desensitized to a level of peanut protein that substantially exceeds the amount typically found in a peanut-contaminated food product, which we believe ranges from as little as a fraction of a peanut to as much as a single peanut (which typically contains between 250 mg and 300 mg of peanut protein). In addition, even if such patients have an allergic reaction, based on the results of our Phase 2 studies of AR101, we believe it is likely to be less severe as a result of treatment with AR101. Both our Phase 2 studies of AR101 and independent scientific research have indicated that clinically meaningful desensitization can be attained through an OIT treatment regimen, independent of sex, age and other demographics.
    - Rapid and Predictable Onset of Action: In both our Phase 2 clinical trials of AR101, a clinically meaningful level of protection was typically achieved by patients in the AR101 treatment group after only 22 weeks of dosing. Independent scientific research has also shown that continued maintenance dosing pursuant to an OIT treatment regimen can confer increased protection over time.
- Attractive Safety Profile: In our Phase 2 studies of AR101, most patients experienced only mild, intermittent side effects commonly associated with food allergies during the up-dosing phase of treatment. The most frequent of these side effects included gastrointestinal symptoms ranging from itching of the lips to vomiting, hives, throat itching or discomfort, and nasal congestion. We believe that many of these side effects are associated with the increases in dosage amounts during the initial up-dosing phase of the treatment regimen. Once patients are desensitized and on maintenance dosing, we believe that they are likely to experience few or no side effects. Of the 55 patients treated with AR101 in our Phase 2 studies, 44 completed the AR101 treatment regimen, with 10 patients discontinuing treatment due to gastrointestinal side effects that occurred in the first two to four weeks, which were resolved, in each case, within one to three weeks after cessation of treatment. In addition, one patient withdrew from the trial due to scheduling issues. All 10 patients who discontinued early had baseline levels of peanut-specific IgE exceeding 100 kU/L. We hypothesize that peanut-specific IgE, which is routinely measured at the allergist office, may be useful in predicting patient experience on AR101, and we are exploring this finding further in Phase 3 trials.
- Convenient Oral Administration: AR101 is designed to be provided to patients as a convenient, orally administered, once daily therapy that is mixed with common age-appropriate foods. Compared to subcutaneous, epicutaneous or sublingual administration, we believe our CODIT approach represents a more convenient and practical method of dosing, particularly in young patients.
- Direct, Targeted Route of Administration: Oral administration of AR101 enables the allergen to interact directly with immune cells in the gastrointestinal tract responsible for mediating the allergic reaction to peanuts. Oral desensitization is believed to work by gradually shifting the balance of the immune system to dampen the allergic response in the case of accidental exposure.
- Compatibility with Current Clinical Practice and Infrastructure: The AR101 up-dosing regimen involves a series of visits to an allergist. This process is similar in many ways to existing regimens for the treatment of non-food allergies, such as pollen and pet dander, which we believe will facilitate adoption by allergists and reimbursement by payors if AR101 is approved.
- CODIT Support Services: We intend to provide physician education, patient guidance and other support services to facilitate the administration of AR101, if approved.

AR101 Clinical Development Program Leverages Historical OIT Studies

Our development of AR101 leveraged the substantial pre-existing independent scientific research on peanut allergy and OIT. In connection with our IND submission, we licensed data from studies conducted at three leading academic

research institutions that demonstrated the potential of using OIT to desensitize peanut allergic patients.

We have also leveraged academic studies that have shown that the daily administration of a relatively low maintenance dose can enable patients to attain and sustain a significant degree of desensitization. For example, in one study, 29 children with peanut allergy completed an OIT up-dosing regimen and then received a 300 mg daily maintenance dose of peanut protein for 12 months. At the end of that period, 27 of the patients were desensitized to exposure of 3,900 mg of peanut protein and the remaining two were desensitized

to exposure of 2,100 mg of peanut protein. Two other studies have also shown that 300 mg maintenance doses can result in consistent desensitization to exposure many times the level of the maintenance dose.

Our clinical trial designs were developed following a review of the academic study protocols described above as well as protocols used in clinical practice. Many of the protocols used in clinical practice have maximum dose levels of several thousand milligrams of peanut protein and use aggressive dose-escalation rates to reach the maximum dose levels quickly. We believe that, as a result, patients under these protocols sometimes receive too much peanut protein too soon and consequently suffer anaphylaxis, contributing to the perception that OIT is not safe. In designing our clinical trials, we incorporated low initial dose levels, a gradual escalation of the dosing and much lower maintenance dose levels. We believe this approach provides for an improved protocol and has the potential to enable patients to safely attain a clinically significant level of desensitization in a reasonable time frame.

We also believe that a successful oral desensitization treatment regimen requires a well-characterized and precisely manufactured drug product. Independent scientific research has shown that the quantity of peanut protein and the relative concentrations of key peanut proteins can vary widely between the different commercially available peanut products that could potentially be used as a source for oral desensitization therapy. These variations could significantly impact the reliability and safety of an oral desensitization treatment regimen. In order to reduce the potential for variability, we chose to use peanut flour solely from the Golden Peanut Company, or GPC, as the basis for AR101. This flour has been used in most of the leading academic studies of peanut allergy OIT and, based on our own testing, shows little variation in the level of peanut protein in different batches of the company's flour, including between batches produced in different years. In order to develop AR101 as an FDA-approvable biological product, we took the further step of characterizing the protein signature of GPC flour. Independent scientific research has identified numerous peanut proteins that are the allergens that cause allergic reactions to peanuts. Three of these proteins appear to be the most significant and representative of the levels of the other proteins. Our characterization of AR101 is based on measuring total protein amount and the concentrations of those three key proteins, as a proxy for the full range of allergenic proteins contained in AR101.

Phase 2 Clinical Trials—ARC001

Clinical Trial Design

Our first clinical trial of AR101, ARC001, was a randomized, multi-center, double-blind, placebo controlled Phase 2 trial of AR101 for the treatment of peanut allergy. Fifty-five patients with confirmed peanut allergy ranging in age from four to 21 years old participated in the trial, which was conducted at eight leading academic medical research centers in the United States. Of the fifty-five patients, 29 received AR101 and 26 received placebo. Patients were required to have experienced a prior allergic reaction that was attributed to peanuts, have elevated levels of anti-peanut protein antibodies in their blood and/or tested positive for peanut allergy on a skin prick test. In addition, patients were required to react, at a dosage of 100 mg of peanut protein or less, in a DBPCFC (double-blind placebo controlled food challenge). A DBPCFC is performed in a clinical setting in two sessions that are usually on two separate days. On each day, the patient is orally administered escalating doses of either a suspected allergenic food or a placebo over time and monitored to see if an allergic reaction is elicited. For example, in the entry DBPCFC for ARC001, patients were administered challenge does of 3 mg, 10 mg, 30 mg and 100 mg of peanut protein 20 to 30 minutes apart in one session and a series of placebo doses on the same schedule in the other session. Neither the patient nor the clinicians overseeing the DBPCFC knew what substance was being administered in a given session. If the patient developed a moderate or stronger allergic response after being administered a dose of peanut protein, then such patient was deemed to have reacted to the food challenge at that dosage level. While in our clinical trials we screened patients for peanut allergy using a DBPCFC because of its sensitivity, we do not anticipate that a DBPCFC will be a requirement for prescribing AR101 as DBPCFCs are not widely used a diagnostic tool in current clinical practice.

The table below shows the escalation of challenge doses in a peanut DBPCFC along with the corresponding cumulative exposure attained at each dose level:

Dose #	Challenge Dose Amount (mg)	Cumulative Exposure (mg)
1	3	3
2	10	13
3	30	43
4	100	143
5	300	443
6	600	1,043
7	1,000	2,043

We selected reactivity at a challenge dose of 100 mg or less on a DBPCFC as an inclusion criterion for ARC001 to enable the study of AR101 in patients who are very sensitive to peanut. In addition, because a patient's sensitivity to peanut protein can fluctuate significantly based on various factors, we believed that using a lower maximum tolerated dose would reduce the likelihood that patients in the trial would pass the exit DBPCFC at 300 mg solely due to natural variations in their sensitivity.

The table below shows the baseline demographics of patients participating in ARC001:

	Active AR101	Placebo
Intent To Treat	29 patients	26 patients[(1)]
Sex	20 male; 9 female	16 male; 10 female
Median Age (min, max)	7 years (4 to 21)	8 years (4 to 14)
Median Peanut Specific IgE (min, max)	64.3 (0.8 to >100)	100.0 (3.5 to >100)
Median Wheal (min, max)	14 mm (5 to 30)	13 mm (5 to 26)
Median Max Tolerated Dose, Cumulative (min, max)	13 mg (3 to 43)	28 mg (3 to 43)

(1) The placebo group initially contained 27 patients, with one patient withdrawing from the study prior to the commencement of treatment.

In ARC001, 29 patients received AR101 and 26 patients received placebo. On the first day of the study, patients were up-dosed to a dose of 3 mg or 6 mg at the clinical site. Patients then took a daily 3 mg or 6 mg dose at home for two weeks and returned to the clinical site to be up-dosed to the next dose level, either 6 mg or 12 mg dose. This process continued with doses of 12 mg, 20 mg, 40 mg, 80 mg, 120 mg, 160 mg, 200 mg, 240 mg and, finally, 300 mg. If a patient had an allergic reaction at a particular level, the allergist could maintain the patient at that dose for a longer period of time or reduce the dose for a period of time before resuming up-dosing. In addition, if a patient's schedule did not allow him or her to visit an allergist's office exactly two weeks after an up-dosing, the patient was permitted to remain on the current dose until he or she was able to visit an allergist. Even with this flexibility, the median completion time for the patients in the AR101 group was not significantly longer than the scheduled completion time. After patients had been taking the 300 mg dose for two weeks, they were administered a DBPCFC with a maximum challenge dose of 600 mg (a 1,043 mg cumulative dose).

Clinical Trial Results and Key Metrics

As the tables below show, ARC001 met the primary endpoint of passing a DBPCFC at a 300 mg challenge dose and met an additional endpoint of passing a DBPCFC at a 600 mg challenge dose.

Primary Endpoint = Pass 300 mg (443 mg cumulative) Challenge at Exit (p<0.0001)				
	Active AR101 (29 patients)		Placebo (26 patients)	
	Patients	%	Patients	%
Responder	23	79%	5	19%
Non-responder	6[(1)]	21%	21	81%

Additional Endpoint = Pass 600 mg (1,043 mg cumulative) Challenge at Exit (p<0.0001)				
	Active AR101 (29 patients)		Placebo (26 patients)	
	Patients	%	Patients	%
Responder	18	62%	0	0%
Non-responder	11[(2)]	38%	26	100%

(1) All were early discontinuations.

(2) Includes the 6 early discontinuations.

Statistical significance is denoted in the table above by reference to the p-values in the Primary Endpoint and Additional Endpoint. The p-value is a measure that states the probability that a comparable or better result would be produced purely by chance. A p-value <0.0001 in the chart means that if the drug was only as effective as the placebo, there would be less than a 0.01% chance that a comparable or better result would be produced purely by chance. A p-value ≤0.05 is a commonly used criterion for statistical significance. When evaluating the potential efficacy of a drug product, the FDA reviews a statistical analysis to determine whether the results of the clinical trial demonstrated that the drug product was efficacious, and a showing of statistical significance in favor of the tested criterion supports the finding of efficacy.

In ARC001, 23 of the 29 patients in the AR101 treatment group completed the trial. All 23 patients who completed the trial passed an exit DBPCFC at a 300 mg challenge dose as compared with five of the 26 patients who received placebo (p <0.0001). In addition, 18 of the 23 patients in the AR101 treatment group that completed the trial passed an

exit DBPCFC at a 600 mg challenge dose compared to none of the 26 patients who received placebo ($p < 0.0001$). Those patients who passed the DBPCFC at a 300 mg challenge dose had received a cumulative dose of 443 mg of peanut protein, the equivalent of approximately one and one half to two peanut kernels, and those patients who passed the DBPCFC at a 600 mg challenge dose had received a cumulative dose of 1,043 mg of peanut protein, the equivalent of approximately four peanut kernels. We believe these results suggest that AR101 has the potential to provide patients with peanut allergy protection from accidental exposure to peanut protein even when taking into account natural variations in sensitivity. Consistent with independent academic research, our results in ARC001 indicate that clinically meaningful desensitization can be attained independent of gender, age and other demographics.

In addition, we believe that AR101 may lessen the severity of a patient's reaction to an accidental exposure. As the charts below indicate, we observed significantly more severe reactions to exposure to peanut protein in the exit DBPCFCs in the placebo group as compared to the AR101 group at the same challenge dose level.

These results are supported by the frequency of use of epinephrine during the entry and exit DBPCFCs. During the entry DBPCFCs, four patients in each of the AR101 group and the placebo group had an allergic reaction severe enough to require the use of epinephrine. In contrast, in the exit DBPCFCs, only two patients in the AR101 group needed epinephrine, while eleven patients in the placebo group were administered epinephrine, including three who required two doses. The epinephrine use in the placebo group was caused by reactions starting at doses as low as 30 mg, while in the AR101 group, both administrations were triggered by moderate reactions at the highest challenge dose of 600 mg.

Among patients in the AR101 treatment group in ARC001, there was one incident of anaphylactic reaction of moderate severity that was treated with epinephrine, and there were no other serious or severe adverse events related to treatment with AR101 in the study. Six of the 29 patients in the AR101 treatment group dropped out of the trial. Four patients dropped out of the trial because of moderate gastrointestinal side effects, such as abdominal discomfort and vomiting, and two dropped out of the trial because of a combination of gastrointestinal side effects and compliance issues. This drop-out rate was consistent with prior academic OIT studies. The patients in ARC001 who discontinued treatment prematurely all began to have gastrointestinal symptoms at the 3, 6 or 12 mg dose level and generally dropped out of the study early. Their gastrointestinal issues resolved without significant medical intervention within one to three weeks. A retrospective analysis revealed that all of these patients had baseline levels of peanut-specific IgE greater than 100 kU/L. One of the patients was diagnosed with eosinophilic esophagitis, or EoE, a condition in which a certain type of white blood cell accumulates in the esophagus. EoE is an immune condition that can be triggered by exposure to food allergens. The standard of care for EoE is simply to avoid exposure to the triggering food allergen, which allows the condition to resolve. Once this patient ceased ingesting AR101, the patient's EoE symptoms resolved within three weeks. No patients in the placebo group dropped out and there were no incidents of anaphylaxis or other severe or serious adverse events related to treatment in the placebo group.

Phase 2 Clinical Trials—ARC002

Patients who completed ARC001 were eligible to participate in our Phase 2 follow-on study, ARC002, an open label study designed to evaluate the long-term safety, efficacy and tolerability of AR101. In ARC002, those patients who had been in the AR101 treatment group for ARC001 were maintained on a 300 mg maintenance dose for three months and then administered a DBPCFC with a maximum challenge dose of 1,000 mg, resulting in a maximum cumulative dose of 2,043 mg. After administration of this DBPCFC, the patients could choose to continue with a 300 mg maintenance dose or to up-titrate to a higher dose level up to a maximum of 2,000 mg per day. Patients who had been in the placebo group in ARC001 began ARC002 by going through the same up-titration regimen that had been administered to the active group in ARC001 and then were placed on a 300 mg maintenance dose for three months. As with the original active group, they were administered DBPCFCs at the end of both the up-titration period and the three-month maintenance period. They then could choose to either stay at a daily dose of 300 mg or begin an up-titration regimen. Independent scientific research has shown that continued maintenance dosing can confer increased protection over time.

Our ARC002 results confirmed and expanded upon the efficacy results of ARC001. All 26 patients from the placebo arm of ARC001 entered ARC002, and 21 completed the up-dosing phase of treatment. Four patients, all with baseline levels of peanut-specific IgE greater than 100 kU/L, dropped out of the study due to gastrointestinal issues similar to those seen in the patients who discontinued treatment in ARC001, and one patient dropped out of the study due to scheduling issues. Twenty of the 21 patients who completed the up-dosing phase passed the post-up-dosing DBPCFC at a challenge dose of 300 mg, or a 443 mg cumulative dose.

A total of 41 patients, 21 from the ARC001 active arm and 20 from the ARC001 placebo arm, entered the three-month maintenance phase of treatment, during which each patient received a daily dose of 300 mg, and were administered a post-maintenance DBPCFC. One patient from the ARC001 active arm did not complete the maintenance period for reasons unrelated to treatment. Of the 40 patients who completed the maintenance period, 100% passed at the 300 mg challenge level, 90% passed at the 600 mg challenge level and 60% passed at the 1,000 mg challenge level. Those patients who passed at the 1,000 mg challenge level had ingested a cumulative dose of 2,043 mg of peanut protein, the equivalent of 7 or 8 peanuts. During the post-maintenance DBPCFCs, two patients required the administration of epinephrine (both after a 1,000 mg challenge dose) and each received only a single administration.

ARC002 also provided additional data regarding the tolerability of AR101. As in ARC001, among the patients who completed the up-dosing phase in ARC002, side effects were generally mild and intermittent. There were no treatment related serious or severe adverse events in any of the ARC002 participants. In addition, the frequency of adverse events during the maintenance period of the ARC002 trial was, on the whole, markedly lower than during the active up-dosing phases of ARC001 and ARC002.

All of the 40 patients who completed the initial portion of the Phase 2 trial volunteered to continue on extended maintenance therapy with AR101. Of these, 11 elected to remain on CODIT maintenance therapy of 300 mg of AR101 per day, and 29 chose to attempt up-dosing to high-dose maintenance therapy. The exposure-adjusted, treatment-related, adverse event rate during extended maintenance for patients on CODIT maintenance therapy was one every 574 days. The exposure-adjusted, treatment-related, adverse event rate during extended maintenance for patients on high-dose maintenance therapy was one every 107 days.

Of the 11 patients who elected to remain on CODIT 300 mg maintenance therapy, 10 remain in the study, and the few adverse events they experienced were almost exclusively mild, with only one categorized as moderate. No patients developed new-onset persistent gastrointestinal symptoms and there were no treatment-related serious adverse events during extended maintenance.

Based on academic studies, we believe that low-dose extended maintenance therapy with AR101 could protect to even higher levels of peanut protein exposure than we saw immediately after up-dosing in ARC001 and after 12 weeks of low-dose maintenance therapy in ARC002. Independent studies have shown that a low, 300 mg daily maintenance dose of peanut protein can achieve a high level of desensitization, as patients in those studies were able to tolerate at least 2,100 mg and as much as 5,000 mg of peanut protein in food challenges administered after a year or more of maintenance therapy. Finally, peanut taste with the CODIT maintenance dose was masked by our AR101 formulation in ARC002, which we expect to support compliance in patients who have peanut taste aversion.

AR101 Phase 3 Development Program

We have developed AR101 in close consultation with the FDA and European regulatory authorities, including the EMA. In September 2014, the FDA granted AR101 Fast-Track designation for OIT of peanut sensitive adults and children and in June 2015, the FDA granted AR101 Breakthrough Therapy designation for OIT of peanut sensitive children and adolescents (ages 4 - 17). These designations are intended to facilitate the development and to expedite the review of drugs and biologics that are intended for the treatment of serious or life-threatening diseases or conditions and, in the case of a Fast-Track designation, that demonstrate the potential to address unmet medical needs for the disease or condition or, in the case of a Breakthrough Therapy designation, where 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. Sponsors of products under development with a Fast-Track designation or Breakthrough Therapy designation may have greater interactions with the FDA, including the involvement of more senior staff members, and the FDA may initiate review of sections of a Fast-Track product's marketing application before the application is complete. A product that receives these designations may be eligible for accelerated approval and priority review, if relevant criteria are met.

We have had ongoing communications and meetings with the FDA relating to the clinical development of AR101 and its manufacture, and we participated in two end-of-Phase 2 meetings with the FDA in July 2015, one with respect to our clinical plans and the other relating to chemistry, manufacturing and control matters. We have had two country level scientific advice meetings with European regulatory authorities and our Pediatric Investigation Plan, or PIP, for AR101 has been approved by the EMA.

PALISADE Trial

In December 2015, we initiated the Phase 3 PALISADE trial, a randomized, double-blind, placebo-controlled study of AR101 for the treatment of peanut allergy in children and adults, which was expected to enroll approximately 500 patients between the ages of 4 and 55 in North America and Europe. The study protocol is largely a combination of the protocols for ARC001 and ARC002. Patients are randomized at a three to one ratio between the AR101 group and a placebo group. Patients are up-dosed to a daily 300 mg dose over a period of five to six months and then maintained at that dose level for approximately six months. At the end of the maintenance period, patients are administered a DBPCFC.

In September 2016, we announced completion of enrollment in the United States and Canada, and, in November 2016, we announced completion of enrollment in Europe. A total of 554 patients were enrolled globally, 90% of whom were between ages 17. We received feedback from the FDA in the first quarter of 2017 that our primary efficacy analysis should be constrained to the 4-17 age group, which aligns with our Breakthrough Therapy Designation patient population. We expect to conduct separate analyses on the adults.

The FDA also provided clarification on the nomenclature used to describe the results of the DBPCFC. Based on this feedback, we will report the single highest tolerated dose in the food challenge as an appropriate and clinically meaningful measure of the results. We will report the primary endpoint of the study as the proportion of patients ages 4-17 tolerating the 600 mg challenge dose in the DBPCFC, which corresponds to a cumulative exposure to 1,043 mg of peanut protein. Secondary endpoints will include tolerating the 300 mg challenge dose, which corresponds to cumulative exposure of 443 mg of peanut protein, and tolerating the 1,000 mg challenge dose, which corresponds to cumulative exposure of 2,043 mg of peanut protein.

We anticipate that up-dosing of patients in PALISADE will be completed around the middle of 2017 and that the study will be completed around year-end 2017. Patients who complete PALISADE will be eligible to participate in a roll-over study, ARC004.

ARC004 Trial

The ARC004 trial is designed to test the durability of AR101 treatment response and dose forgiveness in a multi-arm design to inform the potential for reduced frequency of dosing during the maintenance phase of AR101 therapy. Patients who have completed PALISADE are provided the opportunity to roll over into the ARC004 trial. Patients who were in the AR101 treatment arm in PALISADE will continue to receive AR101 in ARC004. Patients who were in the placebo arm of PALISADE will undergo up-dosing with AR101 in ARC004 and then continue maintenance therapy at the target dose of 300 mg of AR101 per day. The first patient was enrolled into ARC004 in December 2016.

RAMSES Trial

In the second quarter of 2017, we plan to initiate RAMSES, a randomized 2:1, double-blind, placebo-controlled trial, expected to enroll approximately 440 patients between the ages of 4-17 years in the United States and Canada. The RAMSES trial will not require an oral food challenge for entry. Instead, patients will be selected based on stringent entry criteria, including a well-documented medical history of IgE-mediated reactions to peanut (including anaphylaxis), skin prick test reactivity, and assessment of peanut-specific IgE levels. The study will monitor treatment-emergent adverse events during a six-month up-dosing period. Patients will then be followed in an open-label manner for at least six months on the maintenance dose of 300 mg of AR101 per day. We believe the absence of an entry food challenge may further improve the tolerability profile of AR101 in early stages of dosing by removing exposure to high levels of peanut allergen that may otherwise prime the immune system prior to treatment.

Both PALISADE and RAMSES are expected to generate additional data on the potential use of peanut-specific biomarkers to guide treatment decisions with AR101, building on Phase 2 results with AR101 that suggested that baseline levels of peanut-specific IgE may be useful in predicting patient experience on AR101 therapy. In addition, RAMSES will include exploratory analyses on quality of life based on a number of validated patient-reported outcome measures.

ARTEMIS Trial

We are also planning to begin ARTEMIS (AR101 Trial in Europe Measuring oral Immunotherapy Success), a randomized 3:1, double-blind, placebo-controlled trial in peanut-allergic children and adolescents ages 4-17 in Europe that will explore protection at an endpoint of tolerating a single dose of 1,000 mg of peanut protein (corresponding to a cumulative of 2,043 mg peanut protein) after nine months of treatment. The inclusion criteria for the trial will require that patients react at or before the 300 mg dose of the challenge. Patients will undergo approximately six months of up-dosing and then three months of maintenance therapy at 300 mg of AR101 per day, followed by an exit DBPCFC. ARTEMIS builds on the observation that a very high proportion of patients in the ARC002 Phase 2 trial of AR101 were desensitized to more than two grams of peanut protein at the nine-month endpoint. ARTEMIS is designed to confirm that finding in a double-blind, placebo-controlled setting. We expect ARTEMIS to enroll approximately 160 patients at multiple sites in Europe, beginning in mid-2017. We believe that ARTEMIS will help to enhance our knowledge about the timing and extent of desensitization offered by AR101 treatment. As we have engaged with more stakeholders across Europe, we have also come to understand that confirming that a higher efficacy level can be reached sooner would be important in obtaining labeling for protection against accidental exposure and supporting reimbursement applications for AR101, especially as we see increased focus on cost effectiveness throughout Europe.

We expect that an MAA will need to include data from PALISADE, ARC004 and ATEMIS.

ARC005 Trial

Pursuant to our Pediatric Investigation Plan, we are planning on initiating a study of AR101, ARC005, which will include peanut allergic patients ages 1 to 3 in 2018.

ARC008 Trial

All patients exiting RAMSES, ARTEMIS, ARC004 and ARC002 will be eligible to enroll in the ARC008 trial, which provides an opportunity for long-term safety surveillance and for patients to continue maintenance therapy at the target dose of 300 mg of AR101 at the dosing interval the patient had been receiving previously.

Additional Food Allergy Research and Development

We intend to leverage the expertise gained in our development of AR101 to develop CODIT product candidates for a range of additional food allergies. A critical part of our process is transforming natural food products into biopharmaceuticals. This process requires identifying the key proteins that need to be in the product, developing characterizations methods for those proteins, creating usable formulations and ensuring the stability of those formulations.

Leveraging the expertise we have gained developing AR101, we have and expect to continue to conduct activities to support the filing of an IND applicable for a product candidate for the treatment of egg allergy in 2018. We have also initiated pre-clinical development of a product candidate for the treatment of tree nut allergy.

We are also researching potential CODIT product candidates for other food allergies and for the treatment of two or more food allergies at once.

Collaboration with Nestle Health Science

In November 2016, we entered into a two-year strategic collaboration with an affiliate of Nestle Health Science US Holdings, Inc. for the advancement of food allergy therapeutics and issued and sold to Nestle Health Science US Holdings, Inc. (together with its affiliate, Nestle Health Science) 7,552,084 shares of common stock in a private

placement at $19.20 per share, which represented approximately 15.1% of our outstanding shares at the time of the transaction. Subject to certain limited exceptions, Nestle Health Science agreed to a two-year market standoff provision under which it agreed not to sell or transfer any of our common stock or other securities. Subject to certain limited exceptions, Nestle Health Science also agreed to a two-year standstill agreement under which Nestle Health Science agreed not to acquire us through any means. We agreed to register the resale of the shares that Nestle Health Science purchased on a registration statement to be filed with the SEC upon the request of Nestle Health Science, which cannot make the request prior to the 45th day preceding the end of the market standoff provision. The investment and the collaboration do not include any development milestones, product marketing rights or royalties.

The investment launched a two-year strategic collaboration between us and Nestle Health Science, the terms of which enable both parties to discuss our current and future oral immunotherapy development programs through a newly established pipeline forum. Nestle Health Science will provide ongoing scientific, regulatory, and commercial expertise and advice to us through the pipeline forum. Any information disclosed in the collaboration will remain our confidential information, and any new ideas or inventions that arise that relate to our products will be our solely owned intellectual property. If we elect to seek a partner or collaborator for one of

our oral immunotherapy development programs during the two-year term of the collaboration, Nestle Health Science will have a three-month period to negotiate exclusively with us. During the term of the collaboration, and for so long as Nestle Health Science holds not less than ten percent of our outstanding common stock, Nestle Health Science will be entitled to designate one nominee to serve as a director on our Board of Directors. In November 2016, Greg Behar joined our Board of Directors on behalf of Nestle Health Science. The strategic collaboration agreement contains a non-competition covenant pursuant to which Nestle Health Science has agreed not to engage in certain activities relating to OIT for the treatment of food allergies.

Research and Development Expenses

A significant portion of our operating expenses relates to the development of AR101. For the years ended December 31, 2016, 2015, and 2014, our research and development costs were $54.6 million, $19.8 million, and $8.2 million, respectively, and are included in the research and development expense line item in our Consolidated Statements of Operations and Comprehensive Loss. For further detail about the research and development activities, refer to the research and development section in the “Management’s Discussion and Analysis” in this Annual Report on Form 10-K.

Sales and Marketing

Subject to regulatory approval, we intend to commercialize AR101 in the United States and Europe by developing a specialty sales force targeting a subset of the approximately 5,000 practicing allergists in the United States as well as allergy-focused clinicians in major European markets. We anticipate that this sales force could also support the commercialization of additional CODIT product candidates, if approved. We intend to focus our sales efforts on patients with more moderate to severe food allergies, particularly children and adolescents. We do not anticipate that a DBPCFC will be a requirement for prescribing AR101 as DBPCFCs are not widely used as a diagnostic tool in current clinical practice. We anticipate that our CODIT therapeutic approach for food allergies will encompass providing a range of services to patients and their physicians including telephone and e-mail support for patients, physician awareness and education activities, reimbursement assistance, benefit navigation and co-pay and patient assistance programs. Based on the estimated direct medical expenses associated with peanut allergy and the estimated number of people with peanut allergy in the United States, we believe the potential market opportunity for approved peanut allergy treatments in the United States could exceed one billion dollars annually.

Manufacturing

We contract with and rely on third-party manufacturers to produce the food product and final biologic product for our product candidates and to package our product candidates. We have completed construction of a manufacturing facility in a leased building in Clearwater, Florida, at the site of one of our current contract manufacturers. We are installing equipment and qualifying the operating systems in this new facility. We anticipate that this manufacturing facility will be operational by the end of 2017. We plan to continue to rely on the contract manufacturer that is located at the same site to manage the operations of this new manufacturing facility. We also plan to rely on other contract manufacturers for the production of supply for our clinical trials, and if we receive marketing approval for a product candidate, for commercial supply.

Our product candidates are manufactured in accordance with stringent manufacturing processes. Our processes are designed to ensure that that the total protein content of each formulation and the relative concentrations of particular proteins are consistent. Through our contract manufacturers, we are capable of producing dosages with protein content as small as 0.5 mg and have developed advanced analytical methods to ensure each dose contains precisely defined amounts of multiple well-characterized allergenic proteins. Our formulations are also designed to ensure that the drug product is acceptably stable and can be easily mixed with food.

AR101 is currently produced for us by a contract manufacturer using our proprietary process. This process involves several blending and characterization steps intended to ensure that each dose contains a precise amount of peanut flour containing a specific concentration of peanut protein. Because peanut flour is a sensitizing agent, AR101 must be produced on a manufacturing line that is physically separated from other manufacturing lines and that has its own ventilation system. The manufacturing line that we use to produce the clinical supply for our clinical trials will not be adequate to produce commercial supplies of AR101. In June 2015, we leased space in a building near one of our current contract manufacturer's existing facilities and are in the process of establishing a commercial scale manufacturing line for AR101 in that space. We are also in the process of negotiating a supply agreement with our contract manufacturer pursuant to which the manufacturer would use our manufacturing line to produce commercial supplies of AR101 for us. Producing commercial quantities of AR101 will require us to scale up our existing manufacturing process and design and institute rigorous quality control and assurance procedures in our new manufacturing facility. These procedures include qualification of the manufacturing equipment and building utility systems and validation of the manufacturing process at commercial scale. Designing and implementing these procedures are time-consuming and complex operations, which could cause delays in our timelines for bringing this facility into production in 2017. Any delays in bringing this facility online in 2017 could cause a delay in the filing of a BLA or MAA for AR101.

We also rely on separate contract manufacturers to provide packaging services for AR101. We are transitioning from bottles to blister packs as the final packaging configuration for our ongoing and upcoming clinical trials and potential commercial launch of AR101. This transition requires that we implement new manufacturing operations and perform stability testing of AR101 in the blister pack configuration. Any complications with these new operations or the stability testing in the new blister pack configuration could extend the timelines for our planned clinical trials, which would delay the timing of the filing of a BLA or MAA for AR101.

Supplying appropriate clinical trial materials for our ongoing and upcoming clinical trials on a timely basis is a complex operation. There are multiple doses in the up-dosing phase of our AR101 clinical trials. In addition, each subject can proceed through the up-dosing phase at a different rate depending on how the subject responds to each new dose. For example, a subject can move up to the next dose, remain on the current dose or move down to the prior lower dose during the up-dosing phase of our trials. We believe that this dosing flexibility improves outcomes for clinical trial subjects. But this dosing flexibility also increases the complexity of supplying the appropriate doses to each clinical site on a timely basis. We expect that the logistics complexity for our clinical trial materials will increase in 2017 as we initiate several new clinical trials of AR101. In addition, we conduct clinical trials in Europe. EU regulations require that each lot of clinical trial material be certified and released by a designated qualified person, or QP. This certification and release process in the EU can cause delays in supplying clinical trial materials to clinical sites. Any delays or errors in our AR101 supply chain logistics could delay or adversely affect our clinical trials.

Contract manufacturers often encounter difficulties involving production yields, quality control and quality assurance, as well as shortages of qualified personnel. Qualifying manufacturers and providers of packaging services is a lengthy process. If at any time, one or more of our qualified contract organizations were not able to manufacture or package our drug product candidate or provide other requisite services, our business and financial condition could be materially adversely affected.

Our third-party suppliers (other than GPC), their facilities and all lots of product candidates used in our clinical trials are required to be in compliance with current Good Manufacturing Practices, or cGMP. The cGMP regulations include requirements relating to organization and personnel, buildings and facilities, equipment, control of components and drug product containers and closures, production and process controls, packaging and labeling controls, holding and distribution, laboratory controls, records and reports, and returned or salvaged products. The manufacturing facilities for our products must meet cGMP requirements to the FDA’s satisfaction before any product is approved and we can manufacture commercial products. Our third-party manufacturers are also subject to periodic inspections of facilities by the FDA and other authorities, which may include the evaluation of procedures and operations used in the testing and manufacture of our products to assess compliance with applicable regulations.

Suppliers

Our lead product candidate, AR101, contains peanut flour and pharmaceutical-grade ingredients. We source the peanut flour from GPC, a wholly-owned subsidiary of Archer Daniels Midland. We chose to use peanut flour from GPC as the basis for AR101 because its peanut flour has been used in most of the leading academic studies of peanut allergy OIT and because we believe that the widespread use of GPC peanut products in the United States may make their peanut flour representative of the type of peanut protein that patients are most likely to encounter in an accidental exposure. The other ingredients in AR101, such as diluents, glidants and lubricants, are sourced from established producers of pharmaceutical grade ingredients. In order to develop AR101 as an FDA-approvable biological product, we took the further step of characterizing the protein signature of GPC flour. Independent scientific research has identified numerous peanut proteins that are the allergens that cause allergic reactions to peanuts. Three of these proteins appear to be the most significant and representative of the levels of the other proteins. Our characterization of AR101 is based on measuring total protein amount and the relative concentrations of those three key proteins as well as their potencies in an antibody binding assay.

We purchase standard food-grade peanut flour from GPC pursuant to a long-term exclusive commercial supply agreement. Under the terms of the agreement, we are obligated to purchase peanut flour exclusively from GPC provided that GPC is able to supply us in a timely manner with the quantity of peanut flour that we require. GPC is not allowed to sell peanut flour of the type (or equivalent to the type) we use to any third party in United States, Mexico, Canada, the European Union or Japan for use in OIT for peanut allergy provided that we are in compliance with our exclusive purchase obligation and meet specified annual purchase commitments. The agreement remains in effect until five years after the first delivery to us of peanut flour for commercial use and includes an option for us to extend the term for an additional five years. We may terminate the agreement at any time for any reason upon providing 60 days' written notice to GPC, and GPC may terminate the agreement upon 60 days' written notice if we fail to meet our minimum annual purchase commitment and fail to pay an amount equal to GPC's standard price for the unpurchased quantity within the notice period. Either party may terminate the agreement if the other party fails to cure their material breach within 30 days of receiving notice of such breach from the non-breaching party or if the other party fails to perform their obligations under the agreement for a continuous period of 90 days due to a force majeure event or an insolvency or bankruptcy-related events.

Intellectual Property

We have filed patent applications in the United States and international patent applications pursuant to the Patent Cooperation Treaty relating to the manufacture, formulation and stability of AR101 and certain of our other product candidates. Two patents, covering the formulation of and certain of our manufacturing methods for AR101, have been issued in the United States. There is no assurance that any additional patents will be issued from any of our pending patent applications. Even if patents do issue, there can be no assurance that the scope of the claims contained in the patents will be broad enough to provide protection from potentially competing products. If issued, our patents relating to AR101 are projected to expire in 2033 without taking into account any potential patent term extensions. Our patent applications seek protection relating to our formulations, methods of manufacture and improved methods for treating food allergies. We do not own or license, and do not anticipate that we will be able to obtain, a composition of matter patent over the active pharmaceutical ingredient in AR101 or for any other product candidates that are based on widely or readily available food products.

In addition to patents, we rely upon unpatented trade secrets, know-how, and continuing technological innovation to develop and maintain our competitive position. We protect our proprietary information, in part, using confidentiality agreements with our partners, collaborators, contract manufacturers, suppliers, employees and consultants and invention assignment agreements with our employees. We also have confidentiality agreements or invention assignment agreements with our partners and selected consultants. Despite these measures, any of our intellectual property and proprietary rights could be challenged, invalidated, circumvented, infringed or misappropriated, or such intellectual property and proprietary rights may not be sufficient to permit us to take advantage of current market trends or otherwise to provide competitive advantages.

Competition

Our industry is highly competitive and subject to rapid and significant technological change. While we believe that our development experience and scientific knowledge provide us with competitive advantages, we may face competition from large pharmaceutical and biotechnology companies, smaller pharmaceutical and biotechnology companies, specialty pharmaceutical companies, generic drug companies, academic institutions, government agencies and research institutions and others.

Many of our potential competitors may have significantly greater financial, technical and human resources than we have. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Our commercial opportunity could be reduced or eliminated if our competitors develop or market products or other novel technologies that are more effective, safer or less costly than any that will be commercialized by us, or if they obtain regulatory approval for their product candidates more rapidly than we may obtain approval for ours. Our success will be based in part on our ability to identify, develop and manage a portfolio of drugs that are safer, more efficacious and/or more cost-effective than alternative therapies.

Currently there are no approved medical therapies for the treatment of food allergies. We are aware that DBV Technologies S.A., or DBV, has an ongoing Phase 3 program for peanut allergy and is in development for other food allergies based on a patch technology that epicutaneously delivers food allergens to the patient with the goal of desensitizing the patient to the allergens. If AR101 and/or any future product candidate of ours is approved, they may face competition from DBV’s product candidates, if approved.

In addition, we may face competition from allergists who decide to provide OIT and other desensitization therapies to their patients using their own formulations of food allergens and treatment protocols rather than adopting our product candidates or we may face competition from companies that develop their own OIT products, other desensitization therapy products or products intended to prevent the onset of food allergies in infants or young children.

In the future, we may face competition from competitors seeking to use AR101 as a reference product while developing a biosimilar product candidate using the FDA's abbreviated approval pathway for biosimilar products. The abbreviated regulatory pathway, created pursuant to the Biologics Price Competition and Innovation Act of 2009, or BPCIA, establishes legal authority for the FDA to review and approve biosimilar biologics. To be considered a biosimilar, a product candidate must be highly similar to the reference product notwithstanding minor differences in clinically inactive components. In addition, there can be no clinically meaningful differences between the product candidate and the reference product in terms of the safety, purity, and potency of the product. We believe that the relative concentrations of relevant proteins in the peanut flour we source pursuant to our exclusive contract with the GPC are significantly different from the concentrations of proteins found in other commercially available sources of peanut flour, and that a product candidate using different concentrations of such proteins or different proteins might not be considered "highly similar" to AR101 by the FDA. Such a product candidate would not be eligible for the biosimilar approval pathway. However, there can be no guarantee that the FDA would agree with this interpretation.

Under the BPCIA, a reference product may be eligible for a 12-year period of exclusivity starting from the date that the product is first licensed by the FDA pursuant to the approval of a BLA, during which time no approval of a biosimilar product under the abbreviated approval pathway may be made effective. We believe that if the FDA approves a BLA for AR101, AR101 should qualify for this 12-year period of market exclusivity, known as reference product exclusivity, such that no approval of a biosimilar version of our product could become effective prior to the expiration of that 12-year period. However, these exclusivity provisions have been subject to various interpretations that have not yet been fully addressed by the FDA, and there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider AR101 to be eligible for reference product exclusivity, potentially creating the opportunity for competition sooner than anticipated. In addition, even if AR101 were to receive reference product exclusivity, a competitor may seek approval of a product candidate under a full BLA rather than a biosimilar product application. In such a case, although the competitor would not enjoy the benefits of the abbreviated pathway for biosimilar approval created under the BPCIA, the FDA would not be precluded from making effective an approval of the competitor product pursuant to a BLA prior to the expiration of our 12-year period of marketing exclusivity.

Coverage and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we obtain regulatory approval. In the United States and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend in part on the availability of coverage and adequate reimbursement from third-party payors. Third-party payors include government payor programs (such as Medicare and Medicaid in the United States), managed care plans, private health insurers and other organizations. 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. Third-party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the drug products for a particular indication. Third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the studies required to obtain regulatory approvals. In the United States, decisions regarding the extent of coverage and amount of reimbursement to be provided for our products, if approved, will be made on a payor by payor basis. Each payor determines whether or not it will provide coverage for a drug, what amount it will pay for the drug, and on what tier of its formulary the drug will be placed. The drug’s formulary placement generally determines the out-of-pocket costs to a patient in order to obtain the drug and can strongly influence the adoption of a drug by patients and physicians. 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. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products and related services.

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

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

Significant uncertainty also surrounds the reimbursement of allergists for administering the anticipated treatment regimen for AR101 and our other products candidates. In the United States, it is not certain whether the existing medical claim reimbursement codes used to compensate physicians for their time in administering a therapy will be adequate to compensate for a physician's time in administering AR101 up-dosing visits. We may decide to support the creation of new codes and associated reimbursement rates to ensure that clinicians are adequately compensated; however, creation of new codes is a complicated and lengthy process, and we may not be successful in any such efforts. In addition, if a new code is supported by the American Medical Association, or the AMA, there is no guarantee that a third-party payor will provide reimbursement for such code as that decision is solely in the payor's discretion and must be negotiated on a case by case basis between providers and payors. In markets outside of the United States, we will need to evaluate clinician compensation mechanisms in each market to determine whether there is appropriate payment of physicians for administration of the treatment regimens.

Healthcare Reform

In the United States and certain foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system that could affect our future results of operations as we begin to directly commercialize our products.

In particular, there have been and continue to be a number of initiatives at the U.S. federal and state level that seek to reduce healthcare costs. Initiatives to reduce the federal deficit and to reform healthcare delivery are increasing cost-containment efforts. We anticipate that Congress, state legislatures and the private sector will continue to review and assess alternative benefits, controls on healthcare spending through limitations on the growth of private health insurance premiums and Medicare and Medicaid spending, the creation of large insurance purchasing groups, price controls on pharmaceuticals and other fundamental changes to the healthcare delivery system. Any proposed or actual changes could limit or eliminate our spending on development projects and affect our ultimate profitability.

In March 2010, the Affordable Care Act was signed into law, which substantially changed the way healthcare is financed by both governmental and private insurers. The Affordable Care Act, among other things, established: an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents; revised the methodology by which rebates owed by manufacturers for covered outpatient drugs under the Medicaid Drug Rebate Program are calculated; increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program; extended the Medicaid Drug Rebate program to utilization of certain injectable outpatient drugs, as well as prescriptions of individuals enrolled in Medicaid managed care organizations; and required manufacturers to offer 50% point-of-sale discounts on negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D.

We expect that the new Presidential Administration and U.S. Congress will seek to modify, repeal, or otherwise invalidate all, or certain provisions of, the Affordable Care Act. Since its enactment, there have also been other judicial and Congressional challenges to certain aspects of the Affordable Care Act. As a result, there have been delays in the implementation of, and action taken to repeal or replace, certain aspects of the Affordable Care Act. In March 2017, the U.S. House of Representatives introduced legislation known as the American Health Care Act, or the AHCA, which, if enacted, would amend or repeal significant portions of the Affordable Care Act. Among other changes, the AHCA, would repeal the annual fee on certain brand prescription drugs and biologics imposed on manufacturers and importers, eliminate penalties on individuals and employers that fail to maintain or provide minimum essential coverage and create refundable tax credits to assist individuals in buying health insurance. The AHCA would also make significant changes to Medicaid by, among other things, making Medicaid expansion optional for states, repealing the requirement that state Medicaid plans provide the same essential health benefits that are required by plans available on the exchanges, modifying federal funding, including implementing a per capita cap on federal payments to states, and changing certain eligibility requirements. While it is uncertain when or if the provisions in the AHCA will become law, or the extent to which any such changes may impact our business, it is clear

that concrete steps are being taken to repeal and replace certain aspects of the Affordable Care Act.

Individual states in the United States have also become increasingly aggressive 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.

In addition, third-party payors may revise the payment methodologies used to determine reimbursement amounts. This includes annual updates to payments to physicians for the procedures performed using our products, which could directly impact the demand for any of our product candidates that may be approved. By way of example, the Medicare Access and CHIP Reauthorization Act of 2015, or MACRA, ended the use of the statutory formula, and provided for a 0.5% annual increase in payment rates under the Medicare Physician Fee Schedule through 2019, but no annual update from 2020 through 2025. MACRA also introduced a quality payment program under which individual providers with Medicare billings of $30,000 or 100 patient visits per year will be subject to

certain incentives or penalties based on new program quality standards. The quality payment program has two tracks, one known as the merit based incentive payment system for providers in the fee-for service Medicare program, and the advanced alternative payment model for providers in specific care models, such as accountable care organizations. Payment adjustments for the Medicare quality payment program will begin in 2019.

In the future, there may continue to be additional proposals relating to the reform of the United States healthcare system, some of which could further limit the prices we are able to charge for our products candidates, or increase the co-pay obligations of patients. If future legislation were to impose direct governmental price controls and access restrictions, it could have a significant adverse impact on our business. Managed care organizations, as well as Medicaid and other government agencies, continue to seek price discounts. Some states have implemented, and other states are considering, price controls or patient access constraints under the Medicaid program, and some states are considering price-control regimes that would apply to broader segments of their populations that are not Medicaid-eligible. Due to the volatility in the current economic and market dynamics, we are unable to predict the impact of any unforeseen or unknown legislative, regulatory, payor or policy actions, which may include cost containment and healthcare reform measures. Such policy actions could have a material adverse impact on our profitability.

Government Regulation

Government Regulation in the United States

Government authorities in the United States at the federal, state and local level, as well as in foreign countries, extensively regulate, among other things, the research, development, testing, manufacturing, labeling, packaging, promotion, advertising, storage, distribution, marketing, post-approval monitoring and reporting, and export and import of biologics such as those we are developing. We, along with third-party contractors, will be required to navigate the various pre-clinical, clinical and commercial requirements of the governing regulatory agencies of the countries in which we wish to conduct studies or seek approval or licensure of our product candidates. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local, and foreign statutes and regulations require the expenditure of substantial time and financial resources.

Overview of Biologics Regulation in the United States

In the United States, our product candidates are regulated by the FDA as biologics under the Federal Food, Drug, and Cosmetic Act, or the FDCA, the Public Health Service Act, or PHSA, and regulations implemented by the FDA. Section 351(i)(1) of the PHSA defines a biological product (biologic) as a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein (except any chemically synthesized polypeptide), or analogous product applicable to the prevention, treatment, or cure of a disease or condition of human beings. The process required by the FDA before biologic product candidates may be marketed in the United States generally involves the following:

- completion of pre-clinical laboratory tests and animal studies performed in accordance with the FDA's Good Laboratory Practices, or GLP, regulations;
- submission to the FDA of an IND which must become effective before human clinical trials may begin and must be updated annually;
- approval by an independent Institutional Review Board, or IRB, or ethics committee at each clinical site before the trial is initiated;
- performance of adequate and well-controlled clinical trials to establish the safety, purity and potency of the proposed biologic product candidate for its intended purpose;
- preparation, and submission to the FDA, of a BLA after completion of clinical trials;
- a determination by the FDA within 60 days of its receipt of a BLA to file the application for review;
- satisfactory completion of an FDA Advisory Committee review, if applicable;

- satisfactory completion of an FDA pre-approval inspection of the manufacturing facility or facilities at which the proposed product is produced to assess compliance with cGMP requirements, and to assure that the facilities, methods and controls are adequate to preserve the biological product's continued safety, purity and potency; and
- FDA review and approval of the BLA prior to any commercial marketing or sale of the product in the United States.

Pre-clinical Studies and IND Application

Prior to beginning the first clinical trial with a product candidate, we must submit an IND to the FDA. An IND is a request for authorization from the FDA to administer an investigational new drug product to humans. The central focus of an IND submission is

on the general investigational plan and the protocol(s) for clinical trials. The IND also generally includes results of animal and in vitro studies assessing the toxicology, pharmacokinetics, pharmacology, and pharmacodynamic characteristics of the product; chemistry, manufacturing, and controls information; and any available human data or literature to support the use of the investigational product. We filed an IND for AR101 in April 2013 for use in oral desensitization therapy for peanut allergy in children and adults. Because there are no robust animal models of peanut allergy, we did not conduct any pre-clinical efficacy studies of AR101. In addition, because AR101 is based on a food product, the FDA did not require us to submit any pre-clinical toxicology data.

Clinical Trials

An IND must become effective before human clinical trials may begin. An IND will automatically become effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to the proposed clinical trials. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before the clinical trials can begin. Accordingly, submission of an IND may or may not result in the FDA allowing clinical trials to commence.

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with Good Clinical Practices, or GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. Each clinical protocol and any subsequent protocol amendments must be submitted to the FDA as part of the IND, and an IRB at each site where the study is to be conducted must also approve the study. The IRB must monitor the study until completed. There are also requirements governing the reporting of ongoing clinical trials and clinical trial results to public registries. Clinical trials typically are conducted in three or four sequential phases, but the phases may overlap or be combined.

- Phase 1. The investigational product is initially introduced into healthy human subjects or patients with the target disease or condition. These studies are designed to evaluate the safety, dosage tolerance, metabolism and pharmacologic actions of the investigational product in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness.
- Phase 2. The investigational product is administered to a limited patient population to evaluate dosage tolerance and optimal dosage, identify possible adverse side effects and safety risks and preliminarily evaluate efficacy.
- Phase 3. The investigational product is administered to an expanded patient population, generally at geographically dispersed clinical study sites to generate enough data to statistically evaluate dosage, clinical effectiveness and safety, to establish the overall benefit-risk relationship of the investigational product, and to provide an adequate basis for product licensure.
- Phase 4. In some cases, the FDA may condition approval of a BLA for a product candidate on the sponsor's agreement to conduct additional clinical trials after approval. In other cases, a sponsor may voluntarily conduct additional clinical trials after approval to gain more information about the product. Such post-approval studies are typically referred to as Phase 4 clinical trials.

The FDA, the IRB, or the clinical trial 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. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical 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 to certain data from the trial. We may also suspend or terminate a clinical trial based on evolving business objectives and/or competitive climate. Concurrent with clinical trials, companies may complete additional in vitro studies and develop additional information about the biological characteristics of the product candidate, and must finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, must develop methods for testing the safety, purity and potency of the final product. Additionally, appropriate packaging must be selected and tested and

stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

Review and Approval of a BLA

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, detailed information regarding the investigational product is submitted to the FDA in the form of a BLA requesting approval to market the product for one or more indications. The BLA must include all relevant data available from pertinent pre-clinical and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls, and proposed labeling, among other things. Data can come from company-sponsored clinical trials

intended to test the safety and effectiveness of a use of the product, or from a number of alternative sources, including studies initiated by investigators. Under federal law, the submission of most BLAs is subject to an application user fee, and the sponsor of an approved BLA is also subject to annual product and establishment user fees. These fees are typically increased annually. A waiver of user fees may be obtained under certain limited circumstances.

Once a BLA has been submitted, the FDA's goal is to review the application within ten months after it accepts the application for filing, or, if the application relates to an unmet medical need in a serious or life-threatening indication, six months after the FDA accepts the application for filing. The review process is often significantly extended by FDA requests for additional information or clarification. The FDA reviews a BLA to determine, among other things, whether a product is safe, pure and potent and the facility in which it is manufactured, processed, packed, or held meets standards designed to assure the product's continued safety, purity and potency.

Before approving a BLA, the FDA typically will inspect the facility or facilities at which the product is manufactured. The FDA will not approve the application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP requirements. If the FDA determines that the application, manufacturing process or manufacturing facilities are not acceptable, it will outline the deficiencies in the submission and often will request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

The FDA is required to refer an application for a novel product 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.

After the FDA evaluates a BLA and conducts inspections of manufacturing facilities where the investigational product and/or its substance will be produced, the FDA may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application is not ready for approval. A Complete Response Letter may require additional clinical data and/or an additional pivotal Phase 3 trial or trials, and/or other significant, expensive and time-consuming requirements related to clinical trials, pre-clinical trials or manufacturing. Even if such additional information is submitted, the FDA may ultimately decide that the BLA does not satisfy the criteria for approval. The FDA may also approve the BLA with a Risk Evaluation and Mitigation Strategy, or REMS, plan to mitigate risks, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling, development of adequate controls and specifications, or a commitment to conduct one or more post-market studies or clinical trials, and may limit further marketing of the product based on results of these post-marketing studies. Such post-market testing may include Phase 4 trials and surveillance to further assess and monitor the product's safety and effectiveness after commercialization. In addition, once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing regulatory standards is not maintained or if problems occur after the product reaches the marketplace. New government requirements, including those resulting from new legislation, may also be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our products under development.

Expedited Review and Approval Programs

A sponsor may seek approval of its product candidate under programs designed to accelerate FDA's review and approval of new drugs and biological products that meet certain criteria. Specifically, new drugs and biological

products are eligible for Fast-Track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for that disease or condition. For a Fast-Track product, the FDA may consider sections of the BLA for review on a rolling basis before the complete application is submitted if relevant criteria are met. A Fast-Track designated product candidate may also qualify for priority review, under which the FDA sets the target date for FDA action on the BLA at six months after the FDA accepts the application for filing. Priority review is granted when there is evidence that the proposed product would be a significant improvement in the safety or effectiveness of the treatment, diagnosis, or prevention of a serious condition. If criteria are not met for priority review, the application is subject to the standard FDA review period of 10 months after FDA accepts the application for filing. Priority review designation does not change the scientific or medical standard for approval or the quality of evidence necessary to support approval.

Under the accelerated approval program, the FDA may approve a BLA on the basis of either a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or

mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Post-marketing studies or completion of ongoing studies after marketing approval are generally required to verify the biologic's clinical benefit in relationship to the surrogate endpoint or ultimate outcome in relationship to the clinical benefit. In September 2014, the FDA granted AR101 Fast-Track designation.

In 2012, Congress enacted the Food and Drug Administration Safety and Innovation Act, or FDASIA. This law established a new regulatory scheme allowing for expedited review of products designated as "Breakthrough Therapies." 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.

Post-Approval Requirements

Biologics 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, most changes to the approved product, such as adding new indications or other labeling claims are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data. Manufacturers of biologics and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and state agencies for compliance with cGMP requirements, which impose certain procedural and documentation requirements upon us and our third-party manufacturers. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

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

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license 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 the marketing, labeling, advertising, and promotion of biologics. A company may make only those claims relating to safety and efficacy, purity and potency that are approved by the FDA and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability. Failure to comply with these requirements can result in, among other things, adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturers' communications on the subject of off-label use of their products.

Abbreviated Licensure Pathway of Biological Products as Biosimilar or Interchangeable

The Patient Protection and Affordable Care Act, or PPACA, signed into law on March 23, 2010, included the BPCIA, which amended the PHSA and established a regulatory scheme authorizing the FDA to approve biosimilars and interchangeable biosimilars. To date, only four biosimilars have been licensed under the BPCIA, and numerous biosimilars have been approved in Europe. The FDA has issued several guidance documents outlining an approach to review and approval of biosimilars.

Under the BPCIA, a manufacturer may submit an application for licensure of a biologic product that is "biosimilar to" or "interchangeable with" a previously approved biological product or "reference product." In order for the FDA to approve a biosimilar product, it must find that there are no clinically meaningful differences between the reference product and proposed biosimilar product in terms of safety, purity, and potency. For the FDA to approve a biosimilar product as interchangeable with a reference product, the agency must find that the biosimilar product can be expected to produce the same clinical results as the reference product, and (for products administered multiple times) that the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

Under the BPCIA, an application for a biosimilar product may not be submitted to the FDA until four years after the date that the reference product is first licensed by the FDA. In addition, the approval of an application for a biosimilar product may not be made effective by the FDA until 12 years after the date that the reference product is first licensed by the FDA. These exclusivity provisions have been subject to various interpretations that have not yet been fully addressed by the FDA. In addition, even if a product is considered to be a reference product eligible for exclusivity, another company could market a competing version of that product if the FDA approves a full BLA for such product containing the sponsor's own pre-clinical data and data from adequate and well-controlled clinical trials to demonstrate the safety, purity and potency of their product. The BPCIA also created certain exclusivity periods for biosimilars approved as interchangeable products. At this juncture, it is unclear whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies, which are governed by state pharmacy law.

Other Healthcare Laws in the United States

In the United States, our activities are potentially subject to regulation by various federal, state and local authorities in addition to the FDA, including the Centers for Medicare & Medicaid Services, other divisions of the United States Department of Health and Human Services (e.g., the Office of Inspector General), the United States Department of Justice and individual United States Attorney offices within the Department of Justice, and state and local governments. The laws we are subject to include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, physician payment transparency and privacy and security laws and regulations.

The federal Anti-Kickback Statute prohibits, among other things, any person from knowingly and willfully offering, soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual, for an item or service or the purchasing or ordering of a good or service, for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs. The Anti-Kickback Statute is subject to evolving interpretations. In the past, the government has enforced the Anti-Kickback Statute to reach large settlements with healthcare companies based on sham consulting and other financial arrangements with physicians. 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, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act. The majority of states also have anti-kickback laws which establish similar prohibitions and in some cases may apply to items or services reimbursed by any third-party payor, including commercial insurers.

Additionally, the civil False Claims Act prohibits knowingly presenting or causing the presentation of a false, fictitious or fraudulent claim for payment to the United States government. Actions under the False Claims Act may

be brought by the Attorney General or as a qui tam action by a private individual in the name of the government. Violations of the False Claims Act can result in very significant monetary penalties and treble damages. The federal government is using the False Claims Act, and the accompanying threat of significant liability, in its investigation and prosecution of pharmaceutical and biotechnology companies throughout the country, for example, in connection with the promotion of products for unapproved uses and other sales and marketing practices. The government has obtained multi-million and multi-billion dollar settlements under the False Claims Act in addition to individual criminal convictions under applicable criminal statutes. Given the significant size of actual and potential settlements, it is expected that the government will continue to devote substantial resources to investigating healthcare providers' and manufacturers' compliance with applicable fraud and abuse laws.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, also created federal criminal statutes that prohibit among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. 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.

There has also been a recent trend of increased federal and state regulation of payments made to physicians and other healthcare providers. The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the Affordable Care Act, among other things, imposed new reporting requirements on drug manufacturers for payments made by them to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to submit required information may result in civil monetary penalties for all payments, transfers of value or ownership or investment interests that are not timely, accurately and completely reported in an annual submission. Drug manufacturers are required to submit reports to the government by the 90th day of each calendar year. Certain states also mandate implementation of compliance programs, impose restrictions on drug manufacturer marketing practices and/or require the tracking and reporting of marketing expenditures and pricing information as well as gifts, compensation and other remuneration to physicians.

We may also be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology and Clinical Health Act, or HITECH, and their respective implementing regulations, including the final omnibus rule published on January 25, 2013, imposes specified requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to "business associates," defined as independent contractors or agents of covered entities that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways, thus complicating compliance efforts.

Government Regulation in Europe

In the European Economic Area, or EEA, (which is composed of the 28 Member States of the European Union plus Norway, Iceland and Liechtenstein), medicinal products can only be commercialized after obtaining a Marketing Authorization, or MA.

There are two types of MAs:

- The Community MA, which is issued by the European Commission through the Centralized Procedure, based on the opinion of the Committee for Medicinal Products for Human Use, or CHMP, of the EMA, and which is valid throughout the entire territory of the EEA. The Centralized Procedure is mandatory for certain types of products, such as biotechnology medicinal products, orphan medicinal products, and medicinal products that contain a new active substance indicated for the treatment of AIDS, cancer, neurodegenerative disorders, diabetes, auto-immune and viral diseases. The Centralized Procedure is optional for products containing a new active substance not yet authorized in the EEA, or for products that constitute a significant therapeutic, scientific or technical innovation or which are in the interest of public health in the EU. Under the Centralized Procedure the maximum timeframe for the evaluation of a marketing authorization application is 210 days (excluding clock stops, when additional written or

oral information is to be provided by the applicant in response to questions asked by the CHMP). Accelerated evaluation might be granted by the CHMP in exceptional cases, when the authorization of a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. Under the accelerated procedure the standard 210 days review period is reduced to 150 days.

- National MAs, which are issued by the competent authorities of the Member States of the EEA and only cover their respective territory, are available for products not falling within the mandatory scope of the Centralized Procedure. Where a product has already been authorized for marketing in a Member State of the EEA, this National MA can be recognized in another Member States through the Mutual Recognition Procedure. If the product has not received a National MA in any Member State at the time of application, it can be approved simultaneously in various Member States through the Decentralized Procedure.

Under the above described procedures, before granting the MA, the EMA or the competent authorities of the Member States of the EEA make an assessment of the risk-benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

Other regulations

We are also subject to numerous federal, state and local laws relating to such matters as safe working conditions, manufacturing practices, environmental protection, fire hazard control, and disposal of hazardous or potentially hazardous substances. We may incur significant costs to comply with such laws and regulations now or in the future.

Employees

As of December 31, 2016, we had 69 full-time employees. Of these employees, 42 are engaged in research and development. Our employees are not represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Corporate Information

We were founded on June 24, 2011 as a Delaware corporation under the name Allergen Research Corporation. In May 2015, we changed our name to Aimmune Therapeutics, Inc. We completed our initial public offering in August 2015. Our common stock is currently listed on The NASDAQ Global Select Market under the symbol “AIMT.” We are an “emerging growth company” under the Jumpstart Our Business Startups Act of 2012, and therefore we are subject to reduced public company reporting requirements. Our principal executive offices are located at 8000 Marina Blvd, Suite 300, Brisbane, CA 94005 and our telephone number is (650) 614-5220. Our website address is www.aimmune.com. The information on, or that can be accessed through, our website is not incorporated by reference into this Annual Report on Form 10-K or any other filings we make with the U.S. Securities and Exchange Commission, or SEC.

Available Information

We make available on or through our website certain reports and amendments to those reports that we file with, or furnish to, the SEC in accordance with the Securities Exchange Act of 1934, as amended, or the Exchange Act. These include our Annual Reports on Form 10-K, our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act. We make this information available on or through our website free of charge as soon as reasonably practicable after we electronically file the information with, or furnish it to, the SEC. Copies of this information may be obtained at the SEC’s Public Reference Room at 100 F Street, NE, Washington, D.C. 20549. Information on the operation of the Public Reference Room may be obtained by calling the SEC at 1-800-SEC-0330. The SEC maintains a website that contains reports, proxy and information statements, and other information regarding our filings, at www.sec.gov. The information on, or that can be accessed through, our website is not incorporated by reference into this Annual Report on Form 10-K or any other filings we make with the SEC.

Item 1A. Risk Factors.

Our business involves significant risks, some of which are described below. You should carefully consider these risks, as well as the other information in this Annual Report on Form 10-K, including our audited financial statements and the related notes and “Management’s Discussion and Analysis of Financial Condition and Results of Operations.” The occurrence of any of the events or developments described below could have a material adverse effect on our business, results of operations, financial condition, prospects and stock price. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations.

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Risks Related to Our Limited Operating History, Financial Condition and Capital Requirements

We have a limited operating history, have incurred significant losses since our inception and anticipate that we will continue to incur losses for the foreseeable future. We have only one product candidate in clinical trials and no product sales, which, together with our limited operating history, make it difficult to assess our future viability.

We are a clinical-stage biopharmaceutical company with a limited operating history. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of risk. To date, we have focused primarily on developing our Characterized Oral Desensitization Immunotherapy, or CODIT™, therapeutic approach and our lead product candidate, AR101, which is currently our only product in clinical development, and researching additional product candidates. We are not profitable and have incurred losses each year since our inception in June 2011. We have only a limited operating history upon which you can evaluate our business and prospects. In addition, we have limited experience and have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the pharmaceutical industry. We have not generated any revenue from product sales and, as a result, we have incurred significant losses. We incurred a net loss of $80.8 million, and $35.8 million for the years ended December 31, 2016 and 2015, respectively. At December 31, 2016, our accumulated deficit was $134.2 million. We expect to continue to incur losses for the foreseeable future, and we anticipate these losses will increase as we continue our development of, seek regulatory approval for and begin to commercialize AR101, and as we develop other product candidates. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity and working capital.

We will require substantial additional financing to achieve our goals, and a failure to obtain this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our product development, other operations or commercialization efforts.

Since commencing our operations in 2011, substantially all of our efforts have been focused on research, development and the advancement of AR101. As of December 31, 2016, we had capital resources consisting of cash, cash equivalents and investments of $282.5 million. We believe that we will continue to expend substantial resources for the foreseeable future as we continue clinical development, seek regulatory approval for and prepare for the commercialization of AR101, and as we develop other product candidates.

These expenditures will include costs associated with conducting clinical trials, pursuing research and development activities and conducting non-clinical studies, obtaining regulatory approvals, manufacturing and supply, sales and marketing and general operations. In addition, other unanticipated costs may arise. Because the outcome of any clinical trial and/or regulatory approval process is highly uncertain, we may not be able to accurately estimate the actual amounts necessary to successfully complete the development, regulatory approval process and commercialization of AR101 or any other product candidates.

We believe that our existing capital resources will be sufficient to fund our current planned development plan for AR101 and North American and European regulatory submissions. However, our operating plan may change as a result of many factors, including factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity, debt financings or other sources, such as strategic collaborations. Such financing may result in dilution to stockholders, imposition of debt covenants and repayment obligations or other restrictions that may affect our business. If we raise additional capital through strategic collaboration agreements, we may have to relinquish valuable rights to our product candidates including possible future revenue streams. In addition, any fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. Furthermore, even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital due to favorable market conditions or strategic considerations.

Our future funding requirements will depend on many factors, including, but not limited to:

- the time and cost necessary to complete our PALISADE trial and the related roll-over study, ARC004, as well as the time and costs associated with the other planned development activities for AR101 including the initiation and operation of RAMSES, ARTEMIS and ARC008;
    - the number, size and type of additional clinical trials or studies that we choose to initiate or the FDA or a foreign regulatory authority requires us to complete for AR101 prior to or following submission of our Biologics License Application, or BLA, or other marketing approval applications, as well as the cost and time of such trials and studies;
- the time and cost necessary to supply clinical trial materials for our clinical trials and develop a commercial-scale manufacturing process for AR101;
- the time and cost associated with clinical trials and pre-clinical development of other product candidates;

- our ability to obtain regulatory approval for and subsequently commercialize AR101 or any other product candidates we develop;
- sales and marketing costs associated with AR101, if approved, including the cost and timing of developing our sales and marketing capabilities;
- the amount of sales and other revenue from AR101, if approved;
- our ability to achieve sufficient market acceptance, coverage and reimbursement from third-party payors and adequate market share for our product candidates;
- the time and cost associated with designing and implementing quality systems for our product candidates in the United States and Europe;
- the cash requirements of any future acquisitions or discovery of product candidates;
- the time and cost necessary to respond to technological and market developments;
- our ability to attract, hire and retain qualified personnel; and
- our ability to obtain and maintain intellectual property protection for AR101 or any future product candidate and the associated costs of such activities, including for filing, prosecuting, defending and enforcing any patents for AR101 or any future product candidate.

Additional funds may not be available when we need them, on terms that are acceptable to us, or at all.

If adequate funds are not available to us on a timely basis, we may be required to delay, limit, reduce or terminate:

- clinical trials or other development activities for AR101 or any future product candidate;
- our research and development activities; or
- our establishment of sales and marketing capabilities or other activities that may be necessary to commercialize AR101 or any future product candidate.

Our operating results may fluctuate significantly, which makes our future operating results difficult to predict and could cause our operating results to fall below expectations or our guidance.

Our quarterly and annual operating results may fluctuate significantly, which makes it difficult for us to predict our future operating results. These fluctuations may occur due to a variety of factors, many of which are outside of our control and may be difficult to predict, including:

- the timing and cost of, and level of investment in, research, development and commercialization activities relating to our product candidates, which may change from time to time;
- coverage and reimbursement policies with respect to our product candidates, if approved, and potential future drugs that compete with our product candidates;
- the timing and cost of our clinical trials, including the ability to initiate sites, enroll patients in a timely manner and submit or obtain approval of regulatory filings;
- the cost of manufacturing our product candidates, which may vary depending on the quantity of production and the terms of our agreements with manufacturers;
- expenditures that we may incur to acquire, develop or commercialize additional product candidates and technologies;
- the level of demand for our products, if approved, which may vary significantly;
- future accounting pronouncements or changes in our accounting policies; and
- the timing and success or failure of clinical trials for our product candidates or competing product candidates, or any other change in the competitive landscape of our industry, including consolidation among our competitors or partners.

The cumulative effects of these factors could result in large fluctuations and unpredictability in our quarterly and annual operating results. As a result, comparing our operating results on a period-to-period basis may not be meaningful. Investors should not rely on our past results as an indication of our future performance.

This variability and unpredictability could also result in our failing to meet the expectations of industry or financial analysts or investors for any period. If our revenue or operating results fall below the expectations of analysts or investors or below any forecasts we may provide to the market, or if the forecasts we provide to the market are below the expectations of analysts or investors, the price of our common stock could decline substantially. Such a stock price decline could occur even when we have met any previously publicly stated revenue and/or earnings guidance we may provide.

Risks Related to Our Business

We are substantially dependent on the success of AR101 which will require significant additional clinical testing before we can seek regulatory approval and potentially commence commercial sales, and which may not be successful in clinical trials, receive regulatory approval or be successfully commercialized, even if approved.

We currently have no products approved for sale. To date, we have invested substantially all of our efforts and financial resources in the research and development of our CODIT therapeutic approach and AR101, which is currently our only product candidate in clinical development. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the FDA or comparable foreign regulatory authorities, and we may never receive such regulatory approval. Before seeking marketing approval from the FDA, or comparable foreign regulatory authorities, for the sale of AR101, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the product in humans. We cannot be certain that AR101 will successfully demonstrate such properties in clinical trials and, even if it is successful, we may not receive regulatory approval for AR101, or we may receive approval in a limited patient population, or we may experience delays in receiving such regulatory approval. If we do not receive regulatory approval for AR101, we may not be able to continue our operations.

As a result, our prospects, including our ability to finance our operations and generate revenue, will depend largely on the successful development, regulatory approval and commercialization of AR101. We do not expect that such commercialization will occur for at least the next two years, if ever. The clinical and commercial success of AR101 will depend on a number of factors, many of which are out of our control, including the following:

- the results from our ongoing and planned clinical trials, including PALISADE and related roll-over study, and the RAMSES and ARTEMIS trials;
- the frequency and severity of adverse effects experienced by patients treated with AR101;
- the availability, perceived advantages, relative cost, relative safety and relative efficacy of alternative and competing treatments;
- the ability of our third-party manufacturers to manufacture supplies of AR101, including their ability to provide adequate and timely supplies of our clinical trial materials and to develop, validate and maintain a commercial-scale manufacturing process that is compliant with current good manufacturing practices, or cGMP;
    - our ability to maintain our exclusive supply relationship with the Golden Peanut Company, or GPC;
- our ability to demonstrate AR101's safety and efficacy to the satisfaction of the FDA and foreign regulatory authorities;
- whether we are required by the FDA or other foreign regulatory authorities, or choose, to conduct additional clinical trials prior to the approval to market AR101, as well as the cost and time of such trials;
- whether the FDA or other foreign regulatory authorities may disagree with the number, design, size, conduct or implementation of our clinical trials;
- our ability to raise additional capital to fund our development, manufacturing and commercialization activities for AR101;
- the receipt of necessary marketing approvals from the FDA and foreign regulatory authorities;
- the extent and nature of any Risk Evaluation and Mitigation Strategy, or REMS, or foreign equivalent, that may be required in connection with regulatory approval or following regulatory approval;
- whether the FDA may restrict the use of our products to a narrow population;

- our ability to successfully commercialize AR101, if approved for marketing and sale by the FDA or foreign regulatory authorities, whether alone or in collaboration with others;
- our success in educating physicians and patients about the benefits, administration and use of AR101;
- acceptance of AR101 as safe and effective by patients and the medical community;

- the continued prevalence of peanut allergy;
- achieving and maintaining compliance with all regulatory requirements applicable to AR101;
- the effectiveness of our own or any future collaborators' marketing, pricing, coverage and reimbursement, sales and distribution strategies and operations;
- our ability to obtain issued patents that cover AR101 and to enforce such patents and other intellectual property rights to AR101;
- our ability to avoid third-party intellectual property claims; and
- a continued acceptable safety profile of AR101 following approval.

In addition, even though AR101 was granted Breakthrough Therapy designation by the FDA for oral immunotherapy of peanut allergic children and adolescents (ages 4 through 17), we may not experience a faster development, review or approval process compared to conventional FDA procedures. Generally, 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. Breakthrough Therapy status allows us to hold additional meetings with the FDA during the development process and to receive advice from the FDA regarding development and approval for AR101. For example, we have held and we intend to continue to request discussions with the FDA on a number of topics for AR101, including the sufficiency of our clinical data for subjects over 17 years of age to support approval in certain adult subgroups.

The FDA and foreign regulatory authorities have substantial discretion in the approval process and we may be required to expend additional time and resources to obtain an approval, if any, and any approval we may seek may be delayed or prevented or limited to a narrower patient population than we originally target. Despite the time and expense exerted, failure can occur at any stage, and, even if we are able to obtain approval for AR101, such approval may be limited to a certain patient subgroup. Accordingly, we cannot assure our stockholders that we will ever be able to generate revenue through the sale of AR101 or become profitable as a result of such sales. If we are not able to successfully demonstrate the safety and efficacy of AR101 in humans in our clinical trials, obtain regulatory approval for AR101 for the indications we seek and successfully commercialize AR101, or if we are significantly delayed in doing so, our business will be materially harmed.

Clinical drug development involves a lengthy and expensive process with an uncertain outcome, and we may encounter substantial delays in our clinical trials. Furthermore, results of earlier studies may not be predictive of future studies' results.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials and of similar academic research studies. For example, the positive results generated in our Phase 2 clinical trials of AR101 do not ensure that our PALISADE trial will demonstrate similar results. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy despite having progressed through initial clinical trials. A number of companies in the pharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier studies, and we cannot be certain that we will not face similar setbacks. Even if our clinical trials are completed, the results may not be sufficient to obtain regulatory approval or commercial acceptance for our product candidates in the indications that we are seeking or at all.

In addition, we do not know whether our planned or future clinical trials will need to be redesigned, enroll an adequate number of patients on time or be conducted on schedule, if at all. Clinical trials can be delayed or terminated for a variety of reasons, including delay or failure to:

- obtain regulatory approval to commence a clinical trial;
-

reach agreement on acceptable terms with prospective contract research organizations, or CROs, clinical trial sites, and specialized clinical vendors, the terms of which can be subject to extensive negotiation and may vary significantly among CROs, clinical trial sites and vendors;

- obtain institutional review board, or IRB, or foreign equivalent approval at each site;
- recruit suitable patients to participate in a clinical trial, including, in particular, a sufficient number of adult patients to support approval in that patient population;
- have patients complete a clinical trial or return for post-treatment follow-up;

- ensure that clinical sites observe clinical trial protocols, operate in accordance with good clinical practice standards, or continue to participate in a clinical trial;
- address any patient safety concerns that arise during the course of a clinical trial, particularly with respect to the double-blind, placebo-controlled food challenges;
- address any conflicts with new or existing laws or regulations;
- initiate or add a sufficient number of clinical trial sites;
- demonstrate that the manufacturing process for AR101 is adequately controlled to ensure that all product produced meets required quality and regulatory standards;
- manufacture sufficient quantities of product candidate for use in clinical trials; or
- provide clinical trial materials to our clinical sites on a timely basis.

For example, subsequent to filing our Investigational New Drug application, or IND, for AR101, the FDA put the Phase 2 clinical trial on clinical hold in order to obtain additional information regarding our manufacturing process and to request certain changes to the design of the clinical trial. Specifically, the FDA requested information regarding the procedures used to ensure that the drug product was not contaminated, the procedures used to ensure the uniformity and consistency of the drug product, our acceptance procedures for the drug product and the placebo, and procedures to ensure correct dosing. In addition, the FDA requested changes to the clinical trial relating to the stopping rules for the trial, withdrawal criteria for the trial, exclusion criteria for patients, the appearance of the drug and the placebo, and the drug lots used in the trial. We provided the FDA with the information it requested and made agreed-upon changes to the clinical trial. However, complying with the FDA's request resulted in an approximately two-month delay in initiation of the trial.

We rely on CROs, specialized clinical vendors, clinical trial sites and consultants 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 and, as a result, may be subject to unanticipated delays. We are conducting our clinical trials at leading academic allergy research centers in the United States and Europe, as well as at community allergy practices. The number and capacity of such sites is limited and our ability to access the sites may be affected by the number and size of other trials occurring at the same time, including trials sponsored by our competitors. If adequate capacity at these sites is not available, the initiation and pace of our clinical trials may be adversely affected.

Conducting clinical trials in foreign countries, as we are doing for our PALISADE trial and will do for ARTEMIS, presents additional risks that may delay completion of our clinical trials. These risks include a foreign regulatory authority imposing additional requirements prior to the commencement of clinical trials in a foreign country, the failure of physicians or 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, and political and economic risks relevant to such foreign countries. For example, clinical trial materials in the European Union must be certified and released by a designated qualified person, which can delay the release of clinical trial materials to clinical sites in the European Union. In addition, the FDA may determine that our clinical trial results obtained in foreign subjects are not representative of the U.S. patient population and are thus not supportive of a BLA approval in the United States.

Patient enrollment is a significant factor in the timing of clinical trials and is affected by many factors, including the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the clinical trial, the design of the clinical trial, safety, competing clinical trials, and clinicians' and patients' perceptions as to the potential advantages of the drug being studied in relation to other available therapies, including any new drugs or treatments that may be approved for the indications we are investigating.

In addition, certain sub-groups of patients may be more difficult to recruit than others. For example, prior to PALISADE, we enrolled only one patient above the age of 17, and we believe the adult patient population is more difficult to recruit than younger patients. While the primary endpoint of PALISADE will be conducted only in patients ages 4 -17, we intend to evaluate AR101 in older patients in PALISADE; however, the number of patients we have

enrolled above 17 years of age is significantly less than the 4 -17 age group. If the FDA concludes that additional safety and efficacy data is required for the adult patient subgroup or any other age-based subgroup, any approval that we may obtain will not include an indication for patients of such subgroup. If we are not able to recruit patients to participate in our clinical trials in a timely manner, our business and results of operations could be adversely affected.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such studies are being conducted, by an independent Safety Review Board for such clinical trial, or by the FDA or other regulatory

authorities. Such authorities 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, failure to pass inspections of the clinical trial operations or trial site by the FDA or other regulatory authorities, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using the product, changes in governmental regulations or administrative actions, issues with the quality of or the manufacturing process used to produce our clinical trial materials or lack of adequate funding to continue the clinical trial. For example, the protocols for certain of our clinical trials require that patients participate in food challenges where they receive increasing amounts of the food to which they are allergic. In our clinical trials, participation in these food challenges has resulted in allergic reactions severe enough to require treatment with epinephrine. It is possible that patients could have allergic reactions severe enough to require hospitalization or even cause death. In such an event, we could be required to suspend or terminate our clinical trials.

If we experience delays in the completion of, or termination of, any clinical trial of our product candidates, the commercial prospects of our product candidates may be harmed, and our ability to generate product revenues from any of these product candidates will be delayed. In addition, any delays in completing our clinical trials will increase our costs, slow down our product candidate development and approval process, and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences could have a material adverse effect on our business, results of operations, financial condition, prospects, and stock price. In addition, many of the factors that cause or lead to a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

In certain of our clinical trials, we utilize an oral food challenge procedure designed to trigger an allergic reaction, which could be severe or life threatening.

In accordance with our food allergy clinical trial protocols, in certain clinical trials we utilize a double-blind, placebo-controlled food challenge procedure. This consists of giving the offending food protein to patients in order to assess the sensitivity of their food allergy, and thus to assess the safety and efficacy of our product candidates versus placebo. The food challenge protocol is meant to induce objective symptoms of an allergic reaction. These oral food challenge procedures can potentially trigger anaphylaxis, a potentially life-threatening systemic allergic reaction. Even though these procedures are well-controlled, standardized, and performed in highly specialized centers with or near intensive care units, there are inherent risks in conducting a clinical trial of this nature. Such risks may dissuade patients or parents of patients from electing to participate in our clinical trials. In addition, an uncontrolled allergic reaction could potentially lead to a serious or even fatal reaction and any such serious clinical event could potentially adversely affect our clinical development timelines, including a complete clinical hold on our food allergy clinical trials. For instance, we are aware of one clinical trial for a peanut allergy treatment that was terminated by its safety monitoring committee because of severe adverse events arising from the administration of food challenges. We may also become liable to subjects who participate in our clinical trials and experience any such serious or fatal reactions. Any of the foregoing could have a material adverse effect on our business, results of operations, financial condition, prospects, and stock price.

The regulatory approval process is lengthy, time-consuming and inherently unpredictable, and we may experience significant delays in obtaining regulatory approval of AR101, if at all, which would delay the commercialization of AR101, adversely impact our ability to generate revenue, and harm our business and our results of operations.

To gain approval to market a biologic product candidate, such as AR101, we must provide the FDA and foreign regulatory authorities with clinical, non-clinical and manufacturing data that adequately demonstrates to the satisfaction of such regulatory authority the safety, purity, potency and effectiveness of the product for the intended indication applied for in the BLA or other relevant regulatory filing. We have not previously submitted a BLA to the FDA, or similar approval filings to comparable foreign regulatory authorities. A BLA or other relevant regulatory filing must include extensive nonclinical and clinical data and supporting information to establish that the product candidate is safe, pure, potent and effective for each desired indication. The BLA or other relevant regulatory filing

must also include significant information regarding the chemistry, manufacturing and controls for the product.

The FDA or any foreign regulatory bodies can delay, limit or deny approval to market AR101 for many reasons, including:

- our inability to demonstrate to the satisfaction of the FDA that AR101 is safe, pure, potent and effective for the proposed indication or meets similar standards set by foreign authorities;
- the FDA or the applicable foreign regulatory authority may disagree with the interpretation of data from clinical trials;
- our inability to demonstrate that the clinical and other benefits of AR101 outweigh any safety or other perceived risks;
- the FDA or the applicable foreign regulatory authority may require additional nonclinical studies or clinical trials, including trials with additional patients in one or more subgroups or populations who have been administered AR101;
- the CROs that we retain to conduct our clinical trials may take actions outside of our control that materially adversely impact our clinical trials;

- the FDA or the applicable foreign regulatory authority may not approve or may disagree with the formulation, packaging, labeling and/or the specifications of AR101;
- if our BLA, if and when submitted, is reviewed by an advisory committee, the FDA may have difficulties scheduling an advisory committee meeting in a timely manner or the advisory committee may recommend against approval of our application or may recommend that the FDA require, as a condition of approval, additional nonclinical studies or clinical trials, limitations on approved labeling or distribution and use restrictions;
- the FDA or the applicable foreign regulatory authority may require development of a REMS as a condition of approval or post-approval that is more extensive than proposed by us;
- our inability to demonstrate that the manufacturing process for AR101 is adequately controlled to ensure that all product produced meets required quality standards;
- the FDA or the applicable foreign regulatory authority may fail to approve the third-party manufacturers or testing laboratories with which we contract; or
- the potential for approval policies or regulations of the FDA or the applicable foreign regulatory authorities to significantly change in a manner rendering our clinical data insufficient for approval.

Of the large number of drugs and biologics in development, only a small percentage successfully complete the FDA or other regulatory approval processes and are commercialized. In addition, the FDA has never approved a drug for treating food allergy through desensitization and, in particular, has never approved a drug based on efficacy as measured by a double-blind, placebo controlled food challenge, which is the testing mechanism for determining the desensitization efficacy of AR101.

Even if we eventually complete clinical testing and receive approval of a BLA or foreign marketing authorization for AR101, the FDA or the applicable foreign regulatory authority may grant approval contingent on the performance of costly additional clinical trials. The FDA or the applicable foreign regulatory authority may also approve AR101 for a more limited indication and/or a narrower patient population than we originally request, and the FDA or applicable foreign regulatory authority may not approve the labeling that we believe is necessary or desirable for the successful commercialization of AR101. Any delay in obtaining, or inability to obtain, applicable regulatory approval or a regulatory approval for a more limited indication and/or narrower patient population would delay, prevent, or limit commercialization of AR101 and would materially adversely impact our business and prospects.

If we do not receive marketing approval for AR101 or are otherwise not successful in commercializing AR101, or are significantly delayed in doing so, our business will be materially harmed and we may need to curtail or cease operations. We currently have no products approved for sale, and we may never obtain regulatory approval to commercialize AR101.

If we do not achieve our projected development and commercialization goals in the timeframes we announce and expect, the commercialization of AR101 or any future product candidates may be delayed, and our business will be harmed.

For planning purposes, we sometimes estimate the timing of the accomplishment of various scientific, clinical, regulatory and other product development objectives. These milestones may include our expectations regarding the commencement or completion of scientific studies and clinical trials, the submission of regulatory filings, or commercialization objectives. From time to time, we may publicly announce the expected timing of some of these milestones, such as the completion of an ongoing clinical trial, the initiation of other clinical programs, receipt of marketing approval, or a commercial launch of a product. The achievement of many of these milestones may be outside of our control. All of these milestones are based on a variety of assumptions which may cause the timing of achievement of the milestones to vary considerably from our estimates, including:

- our available capital resources or capital constraints we experience;
- the rate of progress, costs and results of our clinical trials and research and development activities, including the extent of scheduling conflicts with participating clinicians and collaborators;
- our ability to identify and enroll patients who meet clinical trial eligibility criteria;

- our receipt of approvals by the FDA and other regulatory authorities and the timing thereof;
- other actions, decisions or rules issued by regulators;
- our ability to access sufficient, reliable and affordable supplies of materials used in the manufacture of our product candidates;
- our ability to manufacture and supply clinical trial materials to our clinical sites on a timely basis;
- the efforts of our collaborators with respect to the commercialization of our products; and

- the securing of, costs related to, and timing issues associated with, product manufacturing as well as sales and marketing activities.

If we fail to achieve announced milestones in the timeframes we expect, the commercialization of AR101 and any future product candidates may be delayed, and our business and results of operations may be harmed.

We rely exclusively on the Golden Peanut Company to provide the source material for AR101 and are exposed to a number of sole supplier risks.

The source material for AR101 is a specific type of peanut flour, which we purchase from GPC pursuant to a long-term exclusive commercial supply agreement. In order to develop AR101 as an FDA-approvable biological product we were required to characterize the protein signature of the flour. We believe the flour produced by GPC has a distinct protein signature that is significantly different from the protein signatures of other commercially available peanut flours and, as a result, it is unlikely that we could use any other peanut flours as the source material for AR101. If GPC became unwilling or unable to supply us with peanut flour, our business and operating results would be materially adversely affected.

In addition, our agreement with GPC does not require GPC to provide us with peanut flour that has a specific protein signature or that meets other potentially relevant pharmaceutical standards. We have tested multiple lots of GPC peanut flour produced in several different years and generally have not identified significant variations in the protein signature between lots. We can provide no assurance that natural variations in the peanuts sourced by GPC, changes in the agricultural practices used to produce the peanuts sourced by GPC, or variations in GPC's manufacturing process will not result in alterations in the protein signature or other characteristics of GPC's peanut flour that would make it unsuitable for use in AR101. If such alterations occurred, we would not be able to manufacture AR101 and our business and operating results would be materially adversely affected. In addition, as our purchases of peanut flour from GPC represent an insignificant portion of GPC's total peanut flour sales, we have only a limited ability to influence GPC's decisions regarding its sourcing of peanuts or methods of producing peanut flour.

Our agreement with GPC restricts it from selling peanut flour of the type (or equivalent to the type) we use to any third party in the United States, Canada, Mexico, the European Union or Japan for use in oral immunotherapy, or OIT, for peanut allergy. The agreement remains in effect until five years after the first delivery to us of peanut flour for commercial use and includes an option for us to extend the term for an additional five years. GPC, however, may terminate the agreement upon 60 days' written notice if we fail to meet our minimum annual purchase commitment and fail to pay an amount equal to GPC's standard price for the unpurchased quantity within the notice period. GPC may also terminate the agreement if we fail to cure a material breach within 30 days of receiving notice of such breach from GPC or if we fail to perform our obligations under the agreement for a continuous period of 90 days due to a force majeure event or an insolvency or bankruptcy-related events. If GPC were to make sales despite the restrictions set forth in the agreement, or terminate the agreement as a result of any of the foregoing or if we were to otherwise lose exclusivity, we could face additional competition from pharmaceutical and biotechnology companies, with considerably more resources and experience than we have, that are researching and selling products designed to treat food allergies or allergies in general.

AR101 may cause undesirable side effects or have other properties that could delay or prevent its regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following its marketing approval, if that occurs.

Undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign regulatory authorities. To date, patients treated with AR101 have experienced drug-related side effects, which mainly include gastrointestinal issues ranging from itching of the lips to vomiting. Results of our trials could reveal a high and unacceptable severity and prevalence of these or other side effects. In such an event, our clinical trials could be suspended or terminated and the FDA or comparable foreign regulatory

authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. The drug-related side effects could affect patient recruitment or the ability of enrolled patients to complete the clinical trial or result in potential product liability claims. Any of these occurrences may harm our business, financial condition and prospects significantly.

In addition, clinical trials by their nature utilize a sample of the potential patient population. With a limited number of subjects and limited duration of exposure in our clinical trials, we cannot be assured that rare and severe adverse effects of AR101 will not be uncovered when a significantly larger number of patients are exposed to the drug. Further, we have not designed our clinical trials to determine the effect and safety consequences of taking AR101 over a multi-year period.

Although we have monitored the subjects in our studies for certain safety concerns and we have not seen evidence of significant safety concerns in our clinical trials, patients treated with AR101 may experience adverse reactions. For instance, in independent research studies, patients receiving OIT for peanut allergy have suffered severe anaphylactic reactions. While we have developed AR101 and its associated treatment regimen in a manner which we believe reduces the risk of adverse reactions, we can provide no assurance that patients administered AR101 will not also suffer severe anaphylactic reactions, including reactions leading to death. For example, in our ARC001 clinical trial, one patient had an allergic reaction that was attributed to AR101 that was severe enough to require the administration of epinephrine and six patients in our ARC001 clinical trial and four patients in our ARC002 clinical trial who received AR101 and who did not achieve desensitization dropped out of the clinical trial early in the treatment regimen due to gastrointestinal side effects. It is possible that the FDA may ask for additional data regarding such matters.

If safety problems are identified prior to approval of AR101, the FDA or other regulatory agencies may not approve AR101, may limit the population it is used in or may require warnings on the label. If AR101 is ultimately approved and we or others later identify undesirable side effects caused by AR101, the FDA or other regulatory agencies may require that we amend the labeling of AR101, require additional warnings, create a medication guide outlining the risks of such side effects for distribution to patients, order us to recall AR101 or even withdraw marketing approval for AR101. In addition, we could be sued and held liable for harm caused to patients and our reputation may suffer. Each of these events could prevent us from achieving or maintaining market acceptance of AR101, if approved, and could have a material adverse effect on our business, results of operations, financial condition, prospects and stock price.

The potential efficacy of AR101, if approved, is dependent upon patient compliance with the prescribed dosing regimen, and failure to adhere to the dosing regimen could increase the potential of a patient experiencing an adverse allergic reaction.

The AR101 treatment regimen, if approved, would require that patients start with a very low dose of AR101 and gradually increase their dose over time. Based on our existing clinical data, we anticipate it will take patients approximately six months to reach a daily dose level of 300 mg of peanut protein. Patients would then continue on a daily 300 mg maintenance dose.

In order to maintain desensitization, patients would need to continue to take a daily 300 mg maintenance dose. The potential efficacy of AR101, if approved, is dependent upon patients complying with the prescribed dosing regimen, including the continued maintenance dosing. Based on our studies and independent studies, we do not believe that the occasional failure to take a dose will affect desensitization. However, in the event a patient fails to follow the prescribed dosing regimen, halts or skips treatment and then restarts the dosing regimen, the likelihood of an adverse allergic reaction to the allergen is greatly increased, as any level of desensitization previously achieved may have dissipated. Further, patients will be required to continue to practice avoidance to peanut exposure and if patients begin to achieve desensitization, it is possible that they may become less vigilant in practicing avoidance and further increase their risk of an accidental exposure. As a result, a lack of patient compliance and the resulting increased likelihood for adverse safety events could have a material adverse effect on our ability to obtain and maintain, if approved, the regulatory approval necessary to commercialize AR101.

Failure to do so would significantly harm our business, results of operations, financial condition, prospects and stock price. In addition, if patients drop out of our clinical trial due to the strict dosing regimen, the likelihood that we will be able to demonstrate clinically meaningful desensitization will be decreased.

We rely on third parties to manufacture our clinical trial materials and intend to rely on third parties to manufacture our commercial drug supply of AR101 and to manufacture nonclinical, clinical and commercial supplies of any future product candidate.

We do not currently have the infrastructure or internal capability to produce our clinical or commercial supply of AR101, and we lack the internal resources and the capability to manufacture any product candidates on a nonclinical, clinical or commercial scale. The FDA and other comparable foreign regulatory authorities must, pursuant to inspections that will be conducted before and after we submit our BLA or relevant foreign regulatory submission, approve our contract manufacturers to manufacture AR101 or any future product candidates.

We have completed construction of a manufacturing facility in a leased building in Clearwater, Florida, at the site of our primary contract manufacturer; however, we do not directly control the manufacturing operations of our contract manufacturers, and we are completely dependent on them for operating that facility and for compliance with cGMP for manufacture of our products and product candidates. If the contract manufacturer operating that facility or our other contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or foreign regulatory authorities, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. In addition, we have no direct control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. Furthermore, all of our contract manufacturers are engaged with other companies to supply and/or manufacture materials or products for such companies, which exposes our manufacturers to regulatory risks for the production of such materials and products. As a result, failure to meet the regulatory requirements for the production of those materials and products may generally affect the regulatory clearance of our contract manufacturers' facilities. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our product candidates or if it withdraws its approval in the future, we may need to find alternative manufacturing facilities, which would negatively impact our ability to develop, obtain regulatory approval for or market our product candidates, if approved.

Further, we rely on separate contract manufacturers to provide packaging services for AR101. We are transitioning from bottles to blister packs as the final packaging configuration for our ongoing and upcoming clinical trials and potential commercial launch of AR101. This transition requires that we implement new manufacturing operations and perform stability testing of AR101 in the blister pack configuration. Any complications with these new operations or the stability testing in the new blister pack configuration could extend the timelines for our planned clinical trials, which would delay the timing of our regulatory filings for AR101.

We intend to rely on a single manufacturer for the production of the drug product used in AR101 and a single contract manufacturer for the commercial packaging of AR101. As a result, we are exposed to risks applicable to our contract manufacturers' business, including their financial, leadership and operational risks. If one of these manufacturers encountered financial difficulties and was unable to continue operating or was acquired by a third party and changed strategic direction, our ability to obtain supplies of AR101 or future product candidates could be materially adversely affected.

We have not yet entered into an agreement with any third-party manufacturers to produce commercial quantities of drug product used in AR101 or the packaging of AR101, and any failure to reach such an agreement and commence the development process for AR101 in a timely manner would delay commercialization of AR101.

We intend to rely on third-party manufacturers to develop a commercial-scale manufacturing process for AR101. While we have identified potential manufacturing partners for the commercial supply of drug product used in AR101 and the packaging of AR101, we have not yet entered into agreements with respect to either supply. Aspects of our manufacturing process for AR101 are complex and our existing manufacturing process will need to be scaled up to meet our anticipated commercial requirements. If we and our third-party manufacturers are not able to develop successfully a commercial manufacturing process or do so in a timely manner, we will not be able to initiate commercialization of AR101 within our estimated timeline, if at all. We anticipate that we will initially be dependent on a single contract manufacturer for the production of the drug product used in AR101 and a single contract manufacturer for the packaging of AR101 and that during such time, our commercialization efforts will be substantially dependent on such contract manufacturers' ability to scale up the manufacturing process for AR101. In addition, we will need to make a substantial investment in property and equipment in order to support the commercial production of AR101. Any delay in making that investment and acquiring the necessary infrastructure could delay commercial production of AR101.

Suppling our ongoing clinical trials and planned clinical trials is a complex operation.

Supplying appropriate clinical trial materials for our ongoing and planned clinical trials on a timely basis is a complex operation. There are multiple doses in the up-dosing phase of our AR101 clinical trials. In addition, each subject can proceed through the up-dosing phase at a different rate depending on how the subject responds to each new dose. For example, a subject can move up to the next dose, remain on the current dose or move down to the prior lower dose during the up-dosing phase of our trials. We believe that this dosing flexibility improves outcomes for clinical trial subjects. But this dosing flexibility also increases the complexity of supplying the appropriate doses to each clinical site on a timely basis. We expect that the logistics complexity for our clinical trial materials will increase in 2017 as we initiate several new clinical trials of AR101. In addition, we conduct clinical trials in Europe. EU regulations require that each lot of clinical trial material be certified and released by a designated qualified person. This certification and release process in the EU can cause delays in supplying clinical trial materials to clinical sites. Any delays or errors in our AR101 supply chain logistics could delay or adversely affect our clinical trials.

We rely on third parties to conduct our clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may be unable to obtain regulatory approval for or commercialize AR101 or any future product candidates.

We do not have the ability to conduct clinical trials independently. We rely and plan to continue to rely on medical institutions, clinical investigators, contract laboratories, collaborative partners and other third parties, such as CROs, specialized clinical vendors and consultants to conduct clinical trials on our product candidates. The third parties with whom we contract for execution of our clinical trials play a significant role in the conduct of these studies and the subsequent collection and analysis of data. However, these third parties are not our employees, and except for contractual duties and obligations, we have limited ability to control the amount or timing of resources that they devote to our programs. Although we rely on these third parties to conduct our clinical trials, we remain responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on these third parties does not relieve us of our regulatory responsibilities.

The FDA and foreign regulatory authorities require us and our third-party contractors to comply with regulations and standards, including regulations commonly referred to as good clinical practices, or GCPs, which are regulations and guidelines enforced by the FDA and foreign regulatory authorities for conducting, monitoring, recording and reporting the results of clinical trials to ensure that the data and results are scientifically credible and accurate, and that the clinical trial subjects are adequately informed of the potential risks of participating in clinical trials. Regulatory authorities enforce these GCPs through periodic inspections of clinical trial sponsors, principal investigators and clinical trial sites. If we or any of 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 or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving our marketing applications. We cannot assure our stockholders that upon inspection by a given regulatory authority, such regulatory authority will determine that any of our clinical trials complies with GCP regulations.

In addition, certain of our clinical trials must be conducted with product produced under current good manufacturing practice, or cGMP, regulations. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. In addition, the execution of clinical trials, and the subsequent compilation and analysis of the data produced, requires coordination among various parties. In order for these functions to be carried out effectively and efficiently, it is imperative that these parties communicate and coordinate with one another. Moreover, these third parties may also have relationships with other commercial entities, some of which may compete with us. In addition, our agreements with third parties may typically be terminated by such third parties upon as little as 30 days' prior written notice or, in certain cases, under certain other circumstances, including our insolvency. If the third parties conducting our clinical trials do not perform their contractual duties or obligations, experience work stoppages, do not meet expected deadlines, terminate their agreements with us or need to be replaced, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical trial protocols or GCPs, or for any other reason, we may need to enter into new arrangements with alternative third parties, which could be difficult, costly or impossible, and our clinical trials may be extended, delayed or terminated or may need to be repeated. If any of the foregoing were to occur, we may not be able to obtain regulatory approval for or commercialize the product candidate being tested in such studies.

Even if AR101 or any future product candidates obtain regulatory approval, they may never achieve market acceptance or commercial success, which will depend, in part, upon the degree of acceptance among clinicians, patients, patient advocacy groups, healthcare payors and the general medical community.

Even if we obtain FDA or other regulatory approvals, AR101 or any future product candidates may not achieve market acceptance among clinicians, patients, patient advocacy groups, healthcare payors and the general medical community. With respect to AR101, which we intend to market as a means of obtaining protection from accidental exposure to peanut protein and not as a cure for peanut allergy, we anticipate that clinicians will continue to recommend that their patients strictly avoid foods that may contain any amount of peanut protein and continue to

carry epinephrine auto-injectors even if the patients have been successfully desensitized with AR101. As a result, if we are unable to persuade clinicians, patients, caregivers and payors that AR101 has therapeutic value when used in conjunction with the practice of avoidance, our sales will be adversely affected.

In addition, we may face challenges in gaining market acceptance as a result of our therapeutic approach, which exposes patients to the exact allergen that poses a risk of causing a severe allergic reaction.

Many clinicians believe that previous oral immunotherapy approaches to the treatment of peanut allergy are too unsafe or unreliable to use in clinical practice. We are also susceptible to changes in the public perception of the safety and efficacy of desensitization treatments. For example, if a competitor's desensitization treatment similar to our own had significant safety issues, perceptions of our products could also be negatively impacted even if our product did not have similar safety issues. If we are unable to convince clinicians and their patients that AR101 is safe and reliable, our sales will be adversely affected.

Furthermore, market acceptance of AR101 or any future product candidates for which we receive approval depends on a number of factors, including:

- the efficacy of the product as demonstrated in clinical trials;
- the frequency and severity of any adverse effects and overall safety profile of the product;
- the clinical indication for which the product is approved including any limitations on the patient population for which it is indicated;
- acceptance by clinicians and patients of the product as a safe and effective treatment and their perceptions of the benefit of the product;
- the evaluation of our products by governmental health technology assessment organizations;
- the relative convenience and ease of administration of our products, including patients' acceptance of the need to take our product candidates mixed with food;
    - patient and parent acceptance of our product's formulation and packaging;
- the willingness of patients to comply with a treatment regimen that requires daily administration of our product candidates on a chronic basis;
- the potential and perceived advantages of our product candidates over current treatment options or alternative treatments, including future alternative treatments;
- the cost of treatment in relation to alternative treatments and willingness to pay for our products, if approved, on the part of clinicians and patients;
- the availability of products and their ability to meet market demand, including a reliable supply for long-term daily treatment;
- the strength of our marketing and distribution organizations;
- the quality of our relationships with patient advocacy groups; sufficient third-party coverage or reimbursement for our product candidates; and
- sufficient third-party payments to clinicians for the procedures necessary to administer product candidates.

Any failure by our product candidates that obtain regulatory approval to achieve market acceptance or commercial success would adversely affect the results of our operations.

AR101, if approved, or any future product candidates may face significant competition and our failure to effectively compete may prevent us from achieving significant market penetration.

The pharmaceutical market is highly competitive and dynamic, and is characterized by rapid and substantial technological development and product innovations. In particular, we compete in the segments of the pharmaceutical, biotechnology and other related markets that address the treatment of food allergies. As a result, we may face competition from many pharmaceutical and biotechnology companies, with considerably more resources and experience than we have, that are researching and selling products designed to treat food allergies or allergies in general. We are aware that DBV Technologies S.A. is developing a treatment for peanut allergy, which is currently being evaluated in a Phase 3 clinical trial. Many of our competitors have materially greater financial, manufacturing, marketing, research and drug development resources than we do. Large pharmaceutical and biotechnology companies in particular have extensive expertise in nonclinical and clinical testing and in obtaining regulatory approvals for drugs. In addition, academic institutions, government agencies and other public and private organizations conducting research may seek patent protection with respect to potentially competitive products or technologies. These organizations may also establish exclusive collaborative or licensing relationships with our competitors. Failure to effectively compete against future products approved for the treatment of peanut allergy could harm our business and results of operations.

In addition, we may face competition from clinicians who provide oral immunotherapy to patients using commercially available source material. If we are unable to convince clinicians, patients and caregivers, that our products have advantages over these self-developed approaches to oral immunotherapy, our business and results of operation could be materially adversely affected.

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AR101 and any future product candidates are regulated as biological products, or biologics, which may subject them to competition sooner than anticipated.

With the enactment of the Biologics Price Competition and Innovation Act of 2009, or BPCIA, as part of the Affordable Care Act, an abbreviated pathway for the approval of biosimilar and interchangeable biological products was created. The abbreviated regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as "interchangeable" based on its similarity to an existing brand product. To be considered biosimilar, a product candidate must be highly similar to the reference product notwithstanding minor differences in clinically inactive components. In addition, there can be no clinically meaningful differences between the product candidate and the reference product in terms of the safety, purity and potency of the product. For the FDA to approve a biosimilar product as interchangeable with a reference product, the agency must find that the biosimilar product can be expected to produce the same clinical results as the reference product, and (for products administered multiple times) that the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. We believe that the concentrations of relevant proteins in the peanut flour we source pursuant to our exclusive contract with GPC are significantly different from the concentrations of proteins found in other commercially available sources of peanut flour, and that a product candidate using different concentrations of such proteins or different proteins might not be considered "highly similar" to AR101 by the FDA. In that case, such a product candidate would not be eligible for the biosimilar approval pathway. However, there can be no guarantee that the FDA would agree with this interpretation. Indeed, the BPCIA is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation and meaning are subject to uncertainty. While it is uncertain when such processes intended to implement the BPCIA may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for our biological product candidates.

Under the BPCIA, no approval of an application for a biosimilar product may be made effective until 12 years after the original branded product is first licensed by the FDA pursuant to the approval of a BLA. We believe that if the FDA approves a BLA for AR101, AR101 should qualify for this 12-year period of market exclusivity, known as reference product exclusivity, such that no approval of a biosimilar version of our product could become effective prior to the expiration of that 12-year period. However, these exclusivity provisions have been subject to various interpretations that have not yet been fully addressed by the FDA, and there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider AR101 to be eligible for reference product exclusivity, potentially creating the opportunity for competition sooner than anticipated. In addition, even if AR101 were to receive reference product exclusivity, a competitor may seek approval of a product candidate under a full BLA rather than a biosimilar product application. In such a case, although the competitor would not enjoy the benefits of the abbreviated pathway for biosimilar approval created under the BPCIA, the FDA would not be precluded from making effective an approval of the competitor product pursuant to a BLA prior to the expiration of our 12-year period of marketing exclusivity.

In addition, the extent to which a biosimilar, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biological products is not yet clear. In particular, it is unclear at this juncture whether products deemed "interchangeable" by the FDA will, in fact, be readily substituted by pharmacies. Such substitution will depend on a number of marketplace and regulatory factors that are still developing.

We currently have no sales organization or distribution network. If we are unable to establish sales capabilities and a distribution network on our own or through third parties, we may not be able to market, sell and distribute AR101, if approved, or any future product candidates or generate product revenue.

We currently do not have a sales organization. In order to commercialize AR101, we will need to build our marketing, sales, distribution, managerial and other non-technical capabilities or make arrangements with third parties to perform these services, and we may not be successful in doing so. If AR101 receives regulatory approval, we expect to

establish a specialty sales organization with technical expertise and supporting distribution capabilities to commercialize our product candidates, which will be expensive and time-consuming.

We have no prior experience in the marketing, sale and distribution of pharmaceutical products and there are significant risks involved in building and managing a sales organization, including our ability to hire, retain, and incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel, and effectively manage a geographically dispersed sales and marketing team. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of these products. Further, given our lack of prior experience in marketing, selling and distributing pharmaceutical products, our estimates of the number of sales representatives needed to commercialize AR101 may be materially less than the actual number of sales representatives required. As such, we may be required to hire substantially more sales representatives to adequately support the commercialization of AR101, which could have a material adverse effect on our business, results of operations, financial condition, prospects and stock price.

We may choose to collaborate with third parties that have direct sales forces or established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems. If we are unable to enter into such arrangements on acceptable terms or at all, we may not be able to successfully commercialize AR101. If we are not successful in commercializing AR101 or any future product candidates, either on our own or through collaborations with one or more third parties, our future product revenue will suffer and we would incur significant additional losses.

Any product candidate that we are able to commercialize may become subject to unfavorable pricing regulations, third-party coverage or reimbursement policies.

Significant uncertainty exists as to the coverage and reimbursement status of any drug candidates for which we obtain regulatory approval. Our ability to commercialize any products successfully in the United States will depend in part on the extent to which adequate coverage and reimbursement for these products becomes available from third-party payors, including government health administration authorities, such as those that administer the Medicare and Medicaid programs, and private health insurers. Third-party payors are generally able to affect the utilization of drugs by a variety of mechanisms, including deciding which medications they will cover, determining the amount they will pay for a product, establishing which formulary tier to place the drug on that may result in, among other things, greater out-of-pocket costs to patients, and creating pre-authorization procedures. A primary trend in the U.S. healthcare industry is cost containment. Coverage, reimbursement, out-of-pocket costs to patients, and pre-authorization requirements may impact the demand for any product for which we obtain marketing approval. Increasingly, third-party payors are requiring that companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. If coverage and reimbursement are not available or are available only at limited levels, we may not be able to successfully commercialize any product candidate that we successfully develop.

There may be significant delays in obtaining coverage and reimbursement for approved products, and coverage may be more limited than the purposes for which the product is approved by the FDA. Moreover, eligibility for reimbursement does not imply that any product will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim payments for new products, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Payment rates may vary according to the use of the product and the clinical setting in which it is used, may be based on payments allowed for lower cost products that are already reimbursed and may be incorporated into existing payments for other services. Net prices for products may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of products from countries where they may be sold at lower prices than in the United States. In the United States, private third-party payors often rely upon Medicare coverage and reimbursement policies and payment limitations in setting their own coverage and reimbursement policies. Our inability to promptly obtain adequate coverage, reimbursement and profitable payment rates from both government funded and private payors for new products that we develop could have a material adverse effect on our business, results of operations, financial condition, prospects and stock price.

In addition, the anticipated treatment regimen for AR101 and our other products candidates requires a clinician to see the patient every two weeks during the up-dosing portion of the regimen. These appointments may take significant time as the patient has to be monitored for two hours after receiving an increased dose. It is not certain whether the existing reimbursement codes that can be appropriately used for these visits adequately compensate clinicians for the time spent on the visits. We may decide to seek the creation of new codes and associated reimbursement rates to ensure that clinicians are adequately compensated; however, creation of new codes is a complicated and lengthy process and we may not be successful in any such efforts. If appropriate codes and compensation are not available, clinicians may be deterred from offering AR101 to their patients and our business and operating results would be adversely affected.

In the past, under the Medicare program, physician payments were updated on an annual basis according to a statutory formula. When the application of the statutory formula for the update factor would have resulted in a decrease in total physician payments, Congress would intervene with interim legislation to prevent the reductions. In April 2015, however, the Medicare Access and CHIP Reauthorization Act of 2015, or MACRA, was signed into law, which repealed and replaced the statutory formula for Medicare payment adjustments to physicians. MACRA provided a permanent end to the annual interim legislative updates that had previously been necessary to delay or prevent significant reductions to payments under the Medicare Physician Fee Schedule. MACRA provided for a 0.5% update from July 1, 2015 through December 31, 2015, and for each calendar year through 2019, after which there will be a 0% annual update each year through 2025. In addition, MACRA required the establishment of the Merit-Based Incentive Payment System, or MIPS, beginning in 2019, under which physicians may receive performance based payment incentives or payment reductions based on their performance with respect to clinical quality, resource use, clinical improvement activities and meaningful use of electronic health records. MACRA also required the Centers for Medicare & Medicaid Services, or CMS, beginning in 2019, to provide incentive payments for physicians and other eligible professionals that participate in alternative payment models, such as accountable care organizations, that emphasize quality and value over the traditional volume-based fee-for-service model. It is unclear what impact, if any, MACRA will have on our business and operating results, but any resulting decrease in payment may result in reduced demand for our product candidates or additional pricing pressures.

Outside of the United States, the regulations that govern marketing approvals, pricing, coverage and reimbursement for new therapeutic products vary widely from country to country. Some countries require approval of the sale price of a product before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain regulatory approval for a product in a particular country, but then be subject to price regulations that delay or prevent our commercial launch of the product and negatively impact the revenue we are able to generate from the sale of the product in that country. We will need to evaluate clinician compensation mechanisms in each market outside of the United States to determine whether any action needs to be taken to allow for payment of physicians for administration of the treatment regimens.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of AR101 or any future product candidates, and our existing insurance coverage may not be sufficient to satisfy any liability that may arise.

We face an inherent risk of product liability as a result of the clinical testing of our product candidates and will face an even greater risk if we commercialize any products. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. In addition, we may be sued if our product fails to protect a patient from exposure to a food allergen. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability and a breach of warranties.

Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates. Even successful defense would require significant financial and management resources.

Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for AR101 or any future product candidates;
- injury to our reputation;
- withdrawal of clinical trial participants;
- costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to clinical trial participants or patients;
- regulatory investigations, product recalls or withdrawals, or labeling, marketing or promotional restrictions;
- loss of revenue; and
- the inability to commercialize AR101 or any future product candidates.

Our inability to obtain and maintain sufficient product liability insurance at an acceptable cost and scope of coverage to protect against potential product liability claims could prevent or inhibit the commercialization of AR101 or any future products we develop. We currently carry product liability insurance covering use in our clinical trials in the amount of $5.0 million in the aggregate. Although we maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions and deductibles, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts. Moreover, in the future, we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses.

If and when we obtain approval for marketing AR101, we intend to expand our insurance coverage to include the sale of AR101. However, we may be unable to obtain this liability insurance on commercially reasonable terms, if at all.

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We will need to significantly increase the size of our organization, and we may experience difficulties in managing growth.

As of December 31, 2016, we had 69 full-time employees. We will need to continue to expand our managerial, operational, finance, clinical, manufacturing, commercial and other resources in order to manage our operations, regulatory filings, manufacturing and supply activities, marketing and commercialization activities, clinical trials and develop and commercialize AR101 or any future product candidates. Our management, personnel, systems and facilities currently in place may not be adequate to support this future growth. Our need to effectively execute our growth strategy requires that we:

- expand our general and administrative, manufacturing, sales, marketing and clinical development organizations;
- identify, recruit, retain, incentivize and integrate additional employees;
- establish the infrastructure necessary to support international operations;
- manage our internal development efforts effectively while carrying out our contractual obligations to third parties; and
- continue to improve our operational, legal, financial and management controls, reporting systems and procedures.

We may be unable to successfully implement these tasks, which could have a material adverse effect on our business, results of operations, financial condition, prospects and stock price.

If we fail to attract and retain senior management, we may be unable to successfully develop AR101 or any future product candidates, conduct our clinical trials and commercialize AR101 or any future product candidates.

Our success depends in part on our continued ability to attract, retain and motivate highly qualified personnel. In particular, we are highly dependent upon our senior management. The loss of services of any of these individuals could delay or prevent the successful development of our product pipeline, completion of our planned clinical trial or the commercialization of AR101 or any future product candidates. Although we have entered into employment agreements with our senior management team, these agreements do not provide for a fixed term of service.

Although we have not historically experienced unique difficulties attracting and retaining qualified employees, we could experience such problems in the future. For example, competition for qualified personnel in the biotechnology and pharmaceuticals field is intense due to the limited number of individuals who possess the skills and experience required by our industry. We will need to hire additional personnel as we expand our clinical development and manufacturing activities. We may not be able to attract and retain quality personnel on acceptable terms or at all. In addition, to the extent we hire personnel from competitors, we may be subject to allegations that they have been improperly solicited or that they have divulged proprietary or other confidential information, or that their former employers own their research output.

We incur significant costs as a result of operating as a public company, and our management devotes substantial time to new compliance initiatives. We may fail to comply with the rules that apply to public companies, including Section 404 of Sarbanes Oxley, which could result in sanctions or other penalties that would harm our business.

As a new public company, we have and will continue to incur significant legal, accounting and other expenses that we did not incur as a private company, including costs resulting from public company reporting obligations under the Exchange Act and regulations regarding corporate governance practices. The listing requirements of The NASDAQ Global Select Market require that we satisfy certain corporate governance requirements relating to director independence, distributing annual and interim reports, stockholder meetings, approvals and voting, soliciting proxies, conflicts of interest and a code of conduct. Our management and other personnel will need to devote a substantial amount of time to ensure that we comply with all of these requirements. Moreover, the reporting requirements, rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. Any changes we make to comply with these obligations may not be sufficient to allow us

to satisfy our obligations as a public company on a timely basis, or at all. These reporting requirements, rules and regulations, coupled with the increase in potential litigation exposure associated with being a public company, could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors or board committees or to serve as executive officers, or to obtain certain types of insurance, including directors' and officers' insurance, on acceptable terms.

In addition, we intend to implement an enterprise resource planning, or ERP, system for our company. An ERP system is intended to combine and streamline the management of our financial, accounting, human resources, sales and marketing and other functions, enabling us to manage operations and track performance more effectively. However, an ERP system would likely require us to complete many processes and procedures for the effective use of the system or to run our business using the system, which may result in substantial costs. Additionally, during the conversion process, we may be limited in our ability to convert any business that we acquire to the ERP. Any disruptions or difficulties in implementing or using an ERP system could adversely affect our controls and harm our business, including our ability to forecast or make sales and collect our receivables. Moreover, such disruption or difficulties could result in unanticipated costs and diversion of management attention.

As a public company, we are subject to Section 404, or Section 404, of the Sarbanes-Oxley Act of 2002, or Sarbanes Oxley, and the related rules of the Securities and Exchange Commission, or SEC, which generally requires our management and independent registered public accounting firm to report on the effectiveness of our internal control over financial reporting. Beginning with the second annual report that we will be required to file with the SEC, Section 404 requires an annual management assessment of the effectiveness of our internal control over financial reporting. However, for so long as we remain an emerging growth company as defined in the JOBS Act, we intend to take advantage of certain exemptions from various reporting requirements that are applicable to public companies that are not emerging growth companies, including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404. Once we are no longer an emerging growth company or, if prior to such date, we opt to no longer take advantage of the applicable exemption, we will be required to include an opinion from our independent registered public accounting firm on the effectiveness of our internal controls over financial reporting. We will remain an emerging growth company until the earlier of (1) December 31, 2020, (2) the last day of the year in which we have total annual gross revenue of at least $1.0 billion, (3) the last day of the year in which we are deemed to be a “large accelerated filer” as defined in Rule 12b-2 under the Securities Exchange Act of 1934, as amended, or the Exchange Act, which would occur if the market value of our common stock held by non-affiliates exceeded $700.0 million as of the last business day of the second fiscal quarter of such year or (4) the date on which we have issued more than $1.0 billion in nonconvertible debt securities during the prior three-year period.

During the course of our review and testing, we may identify deficiencies and be unable to remediate them before we must provide the required reports. We or our independent registered public accounting firm may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting, which could harm our operating results, cause investors to lose confidence in our reported financial information and cause the trading price of our stock to fall. In addition, as a public company we will be required to file accurate and timely quarterly and annual reports with the SEC under the Exchange Act. Any failure to report our financial results on an accurate and timely basis could result in sanctions, lawsuits, delisting of our shares from The NASDAQ Global Select Market or other adverse consequences that would materially harm our business.

If we are not successful in identifying, acquiring or commercializing additional product candidates, our ability to expand our business and achieve our strategic objectives would be impaired.

Although a substantial amount of our effort will focus on the continued clinical testing, potential approval and commercialization of AR101, an important element of our strategy is to expand our product portfolio by identifying, developing and commercializing additional therapies including therapies using our CODIT therapeutic approach. A key component of our CODIT approach is utilizing defined dosages of well-characterized food proteins in order to allow for gradual updosing. This requires manufacturing stable and standardized drug product, which, for naturally occurring food based drug products, can be complex and difficult especially in low doses. Other than AR101, none of our product candidates have been tested in human clinical trials and many of our potential product candidates are still in the discovery stage. In addition, while we intend to evaluate third-party product candidates and technologies for the treatment of food allergies, we currently have no plans to acquire or in-license any specific product candidate. Our efforts to develop, acquire or in-license product candidates may be unsuccessful for many reasons, including:

- we may not be successful in identifying potential product candidates;
- we may not accurately assess the relative technical feasibility or commercial potential of potential product candidates and may not select the most promising product candidates for development, acquisition or in-licensing;
- competitors may develop alternatives that render our product candidates obsolete or less attractive;
- product candidates we develop, acquire or in-license may nevertheless be covered by third-parties' patents or other exclusive rights;
- the market for a product candidate may change over time so that such a product may become unreasonable to continue to develop;
- 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;

- we may have difficulties finding contract manufacturers willing to manufacture our product candidates, which include food allergens;
- a product candidate may not be capable of being produced in clinical or commercial quantities at an acceptable cost, or at all; and
- a product candidate may not be accepted as safe and effective by clinicians, patients, patient advocacy groups, healthcare payors or the general medical community.

If we fail to develop and successfully commercialize other product candidates, our business and future prospects may be harmed and our business will be more vulnerable to any problems that we encounter in developing and commercializing AR101.

Any collaboration arrangements that we may enter into in the future may not be successful, which could adversely affect our ability to develop and commercialize AR101 and potential future product candidates.

We may seek collaboration arrangements with pharmaceutical or biotechnology companies for the development or commercialization of AR101 and other product candidates depending on the merits of retaining commercialization rights for ourselves as compared to entering into collaboration arrangements. We will face, to the extent that we decide to enter into collaboration agreements, significant competition in seeking appropriate collaborators. Moreover, collaboration arrangements are complex and time-consuming to negotiate, document, implement and maintain. We may not be successful in our efforts to establish and implement collaborations or other alternative arrangements should we so chose to enter into such arrangements. The terms of any collaborations or other arrangements that we may establish may not be favorable to us.

Any future collaborations that we enter into may not be successful. The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborations are subject to numerous risks, which may include that:

- collaborators have significant discretion in determining the efforts and resources that they will apply to collaborations;
- 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 their strategic focus due to the acquisition of competitive products, availability of funding or other external factors, such as a business combination that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial, abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates;
- a collaborator with marketing, manufacturing and distribution rights to one or more products may not commit sufficient resources to or otherwise not perform satisfactorily in carrying out these activities;
- we could grant exclusive rights to our collaborators that would prevent us from collaborating with others;
- collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability;
- disputes may arise between us and a collaborator that causes the delay or termination of the research, development or commercialization of our current or future products or that results in costly litigation or arbitration that diverts management attention and resources;
- collaborations may be terminated, and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable current or future products;
- collaborators may own or co-own intellectual property covering our products that results from our collaborating with them, and in such cases, we would not have the exclusive right to develop or commercialize such intellectual property; and

- a collaborator's sales and marketing activities or other operations may not be in compliance with applicable laws resulting in civil or criminal proceedings.

If we engage in acquisitions, we will incur a variety of costs and we may never realize the anticipated benefits of such acquisitions.

Although we currently have no plans to do so, we may attempt to acquire businesses, technologies, services, products or product candidates that we believe are a strategic fit with our business. If we do undertake any acquisitions, the process of integrating an acquired business, technology, service, products or product candidates into our business may result in unforeseen operating difficulties and expenditures, including diversion of resources and management's attention from our core business. In addition, we may fail to retain key executives and employees of the companies we acquire, which may reduce the value of the acquisition or give rise to additional integration costs. Future acquisitions could result in additional issuances of equity securities that would dilute the ownership of existing stockholders. Future acquisitions could also result in the incurrence of debt, contingent liabilities or the amortization of expenses related to other intangible assets, any of which could adversely affect our operating results. In addition, we may fail to realize the anticipated benefits of any acquisition.

Changes in tax law and other developments resulting from the new presidential administration in the United States may have a material adverse effect on our business, financial condition and results of operations.

Changes in laws and policy relating to taxes or trade may have an adverse effect on our business, financial condition and results of operations. Potential tax reforms in the United States may result in significant changes to current U.S. tax rules and regulations. These potential changes may trigger an adverse effect on our business, financial conditions and results of operations.

Although we are unable to predict what, if any, changes in tax law will occur, the 2016 U.S. presidential election introduced a great deal of uncertainty regarding current tax and trade policies, tariffs and government regulations, which if altered could have the potential to create a significant adverse effect on trade between the U.S. and other countries. Overall, changes in international trade relations and changes to U.S. tax or other laws (including new or changes in regulations promulgated by the U.S. Internal Revenue Service and the U.S. Department of the Treasury), such as the imposition of or increase in tariffs or other trade barriers, could materially and adversely impact our effective tax rate, increase our costs and reduce the competitiveness of our products.

If we obtain approval to commercialize AR101 outside of the United States, a variety of risks associated with international operations could materially adversely affect our business.

If we or a collaborator seek to commercialize AR101 outside the United States, we expect that we will be subject to additional risks related to entering into these international markets or business relationships, including:

- different regulatory requirements for drug approvals in foreign countries;
- different approaches by reimbursement agencies regarding the assessment of the cost effectiveness of AR101;
- differing U.S. and foreign drug import and export rules;
- reduced protection for intellectual property rights in certain foreign countries;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- different reimbursement systems for food allergy medications and for clinicians treating food allergy patients;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad;
- potential liability resulting from activities conducted on our behalf by distributors or other vendors we engage; and

- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters.

The results of the United Kingdom's referendum on withdrawal from the European Union may have a negative effect on global economic conditions, financial markets and our business.

In June 2016, a majority of voters in the United Kingdom elected to withdraw from the European Union in a national referendum. The referendum was advisory, and the terms of any withdrawal are subject to a negotiation period that could last at least two years after the government of the United Kingdom formally initiates a withdrawal process. Nevertheless, the referendum has created significant uncertainty about the future relationship between the United Kingdom and the European Union, including with respect to the laws and regulations that will apply as the United Kingdom determines which European Union laws to replace or replicate in the event of a withdrawal. The referendum has also given rise to calls for the governments of other European Union member states to consider withdrawal. These developments, or the perception that any of them could occur, have had and may continue to have a material adverse effect on global economic conditions and the stability of global financial markets, and may significantly reduce global market liquidity and restrict the ability of key market participants to operate in certain financial markets.

We have ongoing business in the United Kingdom and the European Union, including employees in the United Kingdom. Further, our ongoing PALISADE phase 3 clinical trial for AR101 includes clinical sites in the United Kingdom and other European Union member nations and we intend to conduct our ARTEMIS study solely in Europe. Any application for Marketing Authorization, or MA, for AR101 or any other product candidate that we may file in the future must be filed by an entity located in a European Union member nation. The lack of clarity about future United Kingdom laws and regulations, as the United Kingdom determines which European Union laws to replace or replicate in the event of a withdrawal, includes regulations related to clinical trials, marketing authorization for drug products, intellectual property rights and employment and labor matters. A lack of clarity in these areas, which are central to the development of our product candidates in the United Kingdom and the European Union and our ongoing business activities in the United Kingdom, may cause operational and strategic uncertainty for us as we consider the timing of and requirements for approval in the United Kingdom for AR101 and the effect of a potential withdrawal on our employees located in the United Kingdom.

Our business involves the use of hazardous materials and we and our third-party manufacturers and suppliers must comply with environmental laws and regulations, which can be expensive and restrict how we do business.

Our research and development activities and our third-party manufacturers' and suppliers' activities involve the controlled storage, use and disposal of hazardous materials. We and our manufacturers and suppliers are subject to laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous materials. In some cases, these hazardous materials and various wastes resulting from their use are stored at our and our manufacturers' facilities pending their use and disposal. We cannot eliminate the risk of contamination, which could cause an interruption of our commercialization efforts, research and development efforts and business operations, environmental damage resulting in costly clean up and liabilities under applicable laws and regulations governing the use, storage, handling and disposal of these materials and specified waste products. Although we believe that the safety procedures utilized by our third-party manufacturers for handling and disposing of these materials generally comply with the standards prescribed by these laws and regulations, we cannot guarantee that this is the case or eliminate the risk of accidental contamination or injury from these materials. In such an event, we may be held liable for any resulting damages and such liability could exceed our resources and governmental authorities may curtail our use of certain materials and/or interrupt our business operations. Furthermore, environmental laws and regulations are complex, change frequently and have tended to become more stringent. We cannot predict the impact of such changes and cannot be certain of our future compliance. We do not currently carry biological or hazardous waste insurance coverage. Any of the foregoing risks could have a material adverse impact on our business.

Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. The recent global financial crisis caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, such as the recent global financial crisis, could result in a variety of risks to our business, including reduced ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our suppliers, possibly resulting in supply disruption. Any of the foregoing could have a materially adverse impact on our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

We or the third parties upon whom we depend may be adversely affected by earthquakes or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Our corporate headquarters is located in the San Francisco Bay Area, which in the past has experienced severe earthquakes. We do not carry earthquake insurance. Earthquakes or other natural disasters could severely disrupt our operations, and could have a material adverse effect on our business, results of operations, financial condition, prospects and stock price.

If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as our enterprise financial systems or manufacturing resource planning and enterprise quality systems, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place currently are limited and are unlikely to prove adequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business.

Furthermore, our contract manufacturer and integral parties in our supply chain, are operating from single sites, increasing their vulnerability to natural disasters or other sudden, unforeseen and severe adverse events. In particular, the manufacturing facility is located in Florida, which in the past has experienced severe hurricanes. If hurricanes or other natural disasters were to affect our contract manufacturer or our supply chain, it could have a material adverse effect on our business, results of operations, financial condition, prospects and stock price.

Our internal computer systems, or those of our CROs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our drug development programs.

Despite the implementation of security measures, our internal computer systems and those of our CROs and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our drug development programs. 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 regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of our product candidates could be delayed.

Our product development programs for candidates may require substantial financial resources and may ultimately be unsuccessful.

In addition to the development of AR101, we are pursuing development of our other early-stage development programs. Our current early-stage development programs are still in the pre-clinical formulation phase and may not result in product candidates we can advance to the clinical development phase. None of our other potential product candidates have commenced clinical trials, and there are a number of FDA and foreign regulatory requirements that we must satisfy before we can commence these clinical trials. Satisfaction of these requirements will entail substantial time, effort and financial resources, and we may never satisfy these requirements. We have and expect to continue to conduct activities to support filing of an IND for a product candidate for the treatment of egg allergy. We have also initiated pre-clinical development of a product candidate for the treatment of tree nut allergy. Any time, effort and financial resources we expend on our other early-stage development programs may adversely affect our ability to continue development and commercialization of AR101 product candidates, and we may never commence clinical trials of such development programs despite expending significant resources in pursuit of their development. Even if we do commence clinical trials of our other potential product candidates, such product candidates may never be approved by the FDA or the foreign regulatory authorities.

Risks Related to Government Regulation

The regulatory approval process is highly uncertain and we may not obtain regulatory approval for the commercialization of AR101 or any future product candidates.

The research, testing, manufacturing, labeling, approval, selling, import, export, marketing and distribution of biologics are subject to extensive regulation by the FDA and other regulatory authorities in the United States and other countries, which regulations differ from country to country.

Neither we nor any future collaboration partner will be permitted to market AR101 or any future product candidate in the United States until we receive approval of a BLA from the FDA, and we will not be permitted to market AR101 in other countries until similar regulatory approvals are obtained in those countries. We have not submitted an application or obtained marketing approval for AR101 anywhere in the world and will not be able to do so until we complete additional clinical trials. Obtaining regulatory approval of a BLA in the United States and similar applications in other countries can be a lengthy, expensive and uncertain process. In addition, failure to comply with FDA and other applicable United States and foreign regulatory requirements may subject us to administrative or judicially imposed sanctions or other actions, including:

- warning letters;
- civil and criminal penalties;
- injunctions;
- withdrawal of regulatory approval of products;
- product seizure or detention;
- product recalls;
- total or partial suspension of production; and
- refusal to approve pending BLAs or supplements to approved BLAs.

Prior to obtaining approval to commercialize a product candidate in the United States or abroad, we or our collaborators must demonstrate with substantial evidence from well-controlled clinical trials, and to the satisfaction of the FDA or other foreign regulatory authorities, that such product candidates are safe, pure, potent and effective for their intended uses. The number of nonclinical studies and clinical trials that will be required for FDA approval varies depending on the product candidate, the disease or condition that the product candidate is designed to address, and the regulations applicable to any particular product candidate. Results from nonclinical studies and clinical trials can be interpreted in different ways. Even if we believe the nonclinical or clinical data for our product candidates are promising, regulatory authorities may not agree that such data are sufficient to support approval. Administering product candidates to humans may produce undesirable side effects, which could interrupt, delay or halt clinical trials and result in the FDA or other regulatory authorities denying approval of a product candidate for any or all targeted indications.

Regulatory approval of a BLA or equivalent application in other territories is not guaranteed, and the approval process is expensive and may take several years. The FDA and foreign regulatory authorities also have substantial discretion in the approval process, we may be required to expend additional time and resources to obtain an approval, if any, and any approval we may seek may be delayed or prevented. For example, the FDA or other regulatory authorities may require us to conduct additional clinical trials for AR101 either prior to or post-approval, such as additional trials in specific patient subpopulations or to establish a larger safety database of patients who have been administered AR101. The FDA or other regulatory authority may also object to elements of our clinical development program. Despite the time and expense exerted, failure can occur at any stage.

Regulatory authorities can delay, limit or deny approval of a drug candidate for many reasons, including, but not limited to, the following:

- a drug candidate may not be deemed safe or effective;
- the characterization of the active pharmaceutical ingredient and the data to demonstrate adequate control of the manufacturing process may be deemed insufficient;
- regulatory officials may not find the data from nonclinical studies and clinical trials sufficient;
- the regulatory authorities might not approve our third-party manufacturers' processes or facilities; or
- the regulatory authorities may change its approval policies or adopt new regulations.

If AR101 or any future product candidate fails to demonstrate safety and efficacy in clinical trials or does not gain regulatory approval, our business and results of operations will be materially and adversely harmed. Additionally, if the FDA or other regulatory authorities require that we conduct additional clinical trials, place limitations on AR101 in our label, delay approval to market AR101 or limit the use of AR101, our business and results of operations may be

harmed.

Even if we receive regulatory approval for AR101 or any future product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense. Additionally, any product candidates, if approved, could be subject to labeling and other restrictions and market withdrawal, and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products.

Even if a drug is approved, regulatory authorities may still impose significant restrictions on a product's indicated uses or marketing or impose ongoing requirements for potentially costly post-marketing studies. Furthermore, any new legislation addressing drug safety issues could result in delays or increased costs to assure compliance.

If AR101 is approved it will be subject to ongoing regulatory requirements for labeling, packaging, storage, advertising, promotion, sampling, record-keeping and submission of safety and other post-marketing information, including both federal and state requirements in the United States and the requirements of the regulatory agencies in other countries. In addition, manufacturers and manufacturers' facilities are required to comply with extensive regulatory requirements, including ensuring that quality control and manufacturing procedures conform to current cGMP requirements. As such, we and our contract manufacturers are subject to continual review and periodic inspections to assess compliance with cGMP. Accordingly, we and others with whom we work must continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, quality control, and quality assurance. We will also be required to report certain adverse reactions and production problems, if any, to regulatory authorities, and to comply with requirements concerning advertising and promotion for our products. 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 label. As such, we may not promote our products for indications or uses for which they do not have regulatory approval.

If a regulatory authority discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or disagrees with the promotion, marketing or labeling of a product, a regulatory authority may impose restrictions on that product or us, including requiring withdrawal of the product from the market. If we fail to comply with applicable regulatory requirements, a regulatory authority or enforcement authority may:

- issue warning letters;
- impose civil or criminal penalties;
- suspend or withdraw regulatory approval;
- suspend any of our ongoing clinical trials;
- refuse to approve pending applications or supplements to approved applications submitted by us;
- impose restrictions on our operations, including closing our contract manufacturers' facilities; or
- seize or detain products or require a product recall.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response, and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenues from AR101. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be adversely affected. Additionally, if we are unable to generate revenues from the sale of AR101 our potential for achieving profitability will be diminished and the capital necessary to fund our operations will be increased.

If approved, AR101 or any future products may cause or contribute to adverse medical events that we are required to report to regulatory authorities and if we fail to do so we could be subject to sanctions that would materially harm our business.

Some participants in our clinical trials have reported adverse effects after being treated with AR101. For example, in our ARC001 clinical trial, one patient had an allergic reaction that was attributed to AR101 that was severe enough to require the administration of epinephrine and six patients in our ARC001 clinical trial receiving AR101 dropped out

of the trial early in the treatment regimen due to gastrointestinal side effects. If we are successful in completing the development of, obtaining approval for, and commercializing AR101 or any other products, FDA and foreign regulatory authority regulations require that we report certain information about adverse medical events if those products may have caused or contributed to those adverse events. The timing of our obligation to report would be triggered by the date we become aware of the adverse event as well as the nature of the event. We may fail to report adverse events we become aware of within the prescribed timeframe. We may also fail to appreciate that we have become aware of a reportable adverse event, especially if it is not reported to us as an adverse event or if it is an adverse event that is unexpected or removed in time from the use of our products. If we fail to comply with our reporting obligations, the FDA or a foreign regulatory authority could take action, including criminal prosecution, the imposition of civil monetary penalties, seizure of our products or delay in approval or clearance of future products.

Our failure to obtain regulatory approvals in foreign jurisdictions for AR101 would prevent us from marketing AR101 internationally.

In order to market any product in the European Economic Area, or EEA (which is composed of the 28 Member States of the European Union plus Norway, Iceland and Liechtenstein), and many other foreign jurisdictions, separate regulatory approvals are required. In the EEA, medicinal products can only be commercialized after obtaining a MA. Before granting the MA, the European Medicines Agency or the competent authorities of the Member States of the EEA make an assessment of the risk benefit balance of the product on the basis of scientific criteria concerning its quality, safety and efficacy.

The approval procedures vary among countries and can involve additional clinical testing, and the time required to obtain approval may differ from that required to obtain FDA approval. A foreign regulatory authority may impose additional requirements prior to the commencement of clinical trials in one country that were not required in other countries, including the United States. Clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. For example, a foreign regulatory authority may determine that our clinical trial results obtained in U.S. subjects are not representative of foreign patient populations and are thus not supportive of an approval outside of the United States. Approval by the FDA does not ensure approval by regulatory authorities in other countries, and approval by one or more foreign regulatory authorities does not ensure approval by regulatory authorities in other foreign countries or by the FDA. However, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others. The foreign regulatory approval process may include all of the risks associated with obtaining FDA approval. We may not be able to file for foreign regulatory approvals or do so on a timely basis, and even if we do file we may not receive necessary approvals to commercialize our products in any market.

We may be subject to healthcare laws, regulation and enforcement.

Although we do not currently have any products on the market, once we begin commercializing our products, we will be subject to additional healthcare statutory and regulatory requirements and enforcement by the U.S. by the federal government and the states and by the governments of other countries where we conduct our business. The laws that will affect our ability to operate as a commercial organization include:

- the U.S. federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in exchange for or to induce either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs. A person or entity does not need to have actual knowledge of this statute or specific intent to violate it to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the false claims laws;
- U.S. federal false claims laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent;
- U.S. federal criminal laws that prohibit executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters. Similar to the federal Anti- Kickback Statute, a person or entity does not need to have actual knowledge of these statutes or specific intent to violate them to have committed a violation;
- the U.S. federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, which governs the conduct of certain electronic healthcare transactions and protects the security and privacy of protected health information;
- the U.S. federal physician sunshine requirements under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively, 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, information related to payments and other transfers of value to physicians,

other healthcare providers, and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members;

- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers;
- state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources;

- state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures and pricing information; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways, thus complicating compliance efforts; and
- European and other foreign law equivalents of each of the laws, including reporting requirements detailing interactions with and payments to healthcare providers.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities could be subject to challenge under one or more of such laws. The risk of our being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, the exclusion from participation in federal and state healthcare programs and imprisonment, any of which could adversely affect our ability to market our products and adversely impact our financial results.

Further, regulations may change, and any additional regulation could prevent, limit or delay regulatory approval of our product candidates, which could harm our business. For example, in December 2016, the 21st Century Cures Act, or Cures Act, was signed into law. The Cures Act, among other things, is intended to modernize the regulation of biologics and spur innovation, but its ultimate implementation remains unclear. We could also be subject to new international, federal, state or local regulations that could affect our R&D programs and harm our business in unforeseen ways. If this happens, we may have to incur significant costs to comply with such laws and regulations, which will harm our results of operations.

We also 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. Notably, on January 23, 2017, President Trump ordered a hiring freeze for all executive departments and agencies, including the FDA, which prohibits the FDA from filling employee vacancies or creating new positions. Under the terms of the order, the freeze will remain in effect until implementation of a plan to be recommended by the Director for the Office of Management and Budget, or OMB, in consultation with the Director of the Office of Personnel Management, to reduce the size of the federal workforce through attrition. An under-staffed FDA could result in delays in FDA's responsiveness or in its ability to review submissions or applications, issue regulations or guidance or implement or enforce regulatory requirements in a timely fashion or at all. Moreover, 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 and approximate the total costs or savings associated with each new regulation or repealed 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. In addition, on February 24, 2017, President Trump issued an executive order directing each affected agency to designate an agency official as a "Regulatory Reform Officer" and establish a "Regulatory Reform Task Force" to implement the two-for-one provisions and other previously issued executive orders relating to the review of federal regulations; however, 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.

Legislative or regulatory healthcare reforms in the United States may make it more difficult and costly for us to obtain regulatory clearance or approval of our product candidates and to produce, market and distribute our products after clearance or approval is obtained.

From time to time, legislation is drafted and introduced in Congress that could significantly change the statutory provisions governing the regulatory approval, manufacture, and marketing of regulated products or the reimbursement thereof. In addition, FDA regulations and guidance are often revised or reinterpreted by the FDA in ways that may significantly affect our business and our products. Any new regulations or revisions or reinterpretations of existing regulations may impose additional costs or lengthen review times of our product candidates. We cannot determine what effect changes in regulations, statutes, legal interpretation or policies, when and if promulgated, enacted or adopted may have on our business in the future. Such changes could, among other things, require:

- additional clinical trials to be conducted prior to obtaining approval;
- changes to manufacturing methods;
- recall, replacement or discontinuance of one or more of our products; and
- additional record keeping.

Each of these would likely entail substantial time and cost and could materially harm our business and our financial results. In addition, delays in receipt of or failure to receive regulatory clearances or approvals for any future products could have a material adverse effect on our business, results of operations, financial condition, prospects and stock price.

In addition, the full impact of recent healthcare reform and other changes in the healthcare industry and in healthcare spending is currently unknown, and may adversely affect our business model. In the United States, the Affordable Care Act was enacted in 2010 with a goal of reducing the cost of healthcare and substantially changing the way healthcare is financed by both government and private insurers. The Affordable Care Act, among other things, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations, established annual fees and taxes on manufacturers of certain branded prescription drugs, and created 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 drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturer’s outpatient drugs to be covered under Medicare Part D.

We expect that the new Presidential Administration and U.S. Congress will seek to modify, repeal, or otherwise invalidate all, or certain provisions of, the Affordable Care Act. Since its enactment, there have also been other judicial and Congressional challenges to certain aspects of the Affordable Care Act. As a result, there have been delays in the implementation of, and action taken to repeal or replace, certain aspects of the Affordable Care Act. In March 2017, the U.S. House of Representatives introduced legislation known as the American Health Care Act, or the AHCA, which, if enacted, would amend or repeal significant portions of the Affordable Care Act. Among other changes, the AHCA, would repeal the annual fee on certain brand prescription drugs and biologics imposed on manufacturers and importers, eliminate penalties on individuals and employers that fail to maintain or provide minimum essential coverage and create refundable tax credits to assist individuals in buying health insurance. The AHCA would also make significant changes to Medicaid by, among other things, making Medicaid expansion optional for states, repealing the requirement that state Medicaid plans provide the same essential health benefits that are required by plans available on the exchanges, modifying federal funding, including implementing a per capita cap on federal payments to states, and changing certain eligibility requirements. While it is uncertain when or if the provisions in the AHCA will become law, or the extent to which any such changes may impact our business, it is clear that concrete steps are being taken to repeal and replace certain aspects of the Affordable Care Act.

In addition, other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. These changes include the Budget Control Act of 2011, which resulted in aggregate reductions of

Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2025 unless additional Congressional action, as well as the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Recently there has also been heightened government scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed bills designed to, among other things, reform government program reimbursement methodologies.

It is likely that federal and state legislatures within the United States and foreign governments will continue to consider changes to existing healthcare legislation. We cannot predict the reform initiatives that may be adopted in the future or whether initiatives that have been adopted will be repealed or modified. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare may adversely affect the demand for any

drug products for which we may obtain regulatory approval, our ability to set a price that we believe is fair for our products, our ability to obtain adequate coverage and reimbursement approval for a product, our ability to generate revenues and achieve or maintain profitability, and the level of taxes that we are required to pay.

Neither a Fast-Track designation nor a Breakthrough Therapy designation by the FDA may actually lead to a faster development or regulatory review or approval process.

Even though we do have Fast-Track designation for AR101 for oral immunotherapy of peanut sensitive adults and children and Breakthrough Therapy designation for AR101 for oral immunotherapy of peanut sensitive children and adolescents (ages 4-17), we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw Fast-Track designation or Breakthrough Therapy designation if it believes that the designation is no longer supported by data from our clinical development program or other sources.

Risks Related to Intellectual Property

If we are unable to obtain and maintain adequate intellectual property protection for AR101 or any future product candidates, we may not be able to compete effectively in our market.

Our commercial success depends in part on our ability to obtain and maintain proprietary or intellectual property protection in the United States and other countries for AR101 and any future product candidates. We intend to rely upon a combination of patents, trademarks, trade secrets and confidentiality agreements to protect our product candidates. Evaluating the strength of patents in the biotechnology and pharmaceutical fields involves complex legal and scientific questions and, as a result, the patent position of biopharmaceutical companies can generally be highly uncertain. Further, any disclosure to or misappropriation by third parties of our confidential or proprietary information could enable competitors to quickly duplicate or surpass our technological achievements, thus eroding our competitive position in our market.

The degree of patent protection we require to successfully commercialize our product candidates may be unavailable or severely limited in some cases and may not adequately protect our rights or permit us to gain or maintain any competitive advantage. Though we currently own two issued patents in the United States covering certain of our manufacturing methods and the formulation for AR101, we do not anticipate that we will be able to obtain a composition of matter patent over the active pharmaceutical ingredient in AR101 or for any other product candidates that are based on widely or readily available food products. We have filed additional patent applications that relate to the manufacture, formulation, stability and other aspects of AR101 and certain of our other product candidates. We cannot assure our stockholders that these applications will result in any additional issued patents in the U.S. or foreign countries. Even if any such additional patents issue, we cannot assure our stockholders that they or any other patents we obtain will include any claims with a scope sufficient to protect AR101 or any other future product candidate or otherwise provide us with meaningful protection or competitive advantage.

The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. 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 drug candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. If we encounter delays in our clinical trials or other delays during the regulatory approval process, even if we obtain patents covering AR101 or other product candidates, the period of time during which we could exclusively market AR101 or such other product candidates under such patents would be reduced. As a result, any

patents we obtain may not provide us with adequate and continuing patent protection sufficient to exclude others from commercializing products similar or identical to our product candidates, including generic versions of such products.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and therefore, to the extent that we acquire patent protection with respect to AR101 or other product candidates, third parties may still challenge our patents in the courts or patent offices in the United States and abroad. Any issued patents we obtain could be narrowed, invalidated, held unenforceable or circumvented, any of which could limit our ability to prevent competitors and other third parties from developing and marketing similar products or limit the length of terms of patent protection we may obtain for our product candidates. Competitors or other third parties may also claim that they invented the inventions claimed in our patent applications, or any patents that may issue in the future, prior to us, or may file patent applications before we do. Further, our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets. Such challenges may also result in our inability to manufacture or commercialize our future products, including AR101, without infringing third-party patent rights. If the breadth or

strength of protection provided by any patents we obtain with respect to AR101 or any future product candidates is successfully challenged, then our ability to commercialize AR101 or any future product candidates could be negatively affected, and we may face unexpected competition that could have a material adverse impact on our business.

Even if they are unchallenged, any patents issuing from our pending patent applications may not adequately protect our intellectual property or prevent others from designing around our claims to circumvent those patents by developing similar or alternative technologies or drugs in a non-infringing manner. For example, a third party may develop a competitive product that provides benefits similar to AR101 or a future product candidate but falls outside the scope of our patent protection. If the patent protection covering 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.

In addition, we may in the future be subject to claims by our former employees or consultants asserting an ownership right in our patents or patent applications, as a result of the work they performed on our behalf. Although we generally require all of our employees, consultants and advisors and any other third parties who have access to our proprietary know-how, information or technology to assign their inventions to us, we cannot be certain that we have executed such agreements with all parties who may have contributed to our intellectual property, nor can we be certain that our agreements with such parties will be upheld in the face of a potential challenge, or that they will not be breached, for which we may not have an adequate remedy.

We may become subject to claims alleging infringement of third-party patents or proprietary rights, the outcome of which could result in delay or prevent the development and commercialization of AR101 or any future product candidates or otherwise prevent us from competing effectively in our market.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell our drug candidates and use our proprietary technologies without infringing or otherwise violating the proprietary rights and intellectual property of third parties. The biotechnology and pharmaceutical industries are characterized by extensive and frequent litigation regarding patents and other intellectual property rights. Third parties, including our competitors, may initiate legal proceedings against us or our collaborators alleging that we are infringing or otherwise violating their patent or other intellectual property rights. Given the vast number of patents in our field of technology, we cannot assure our stockholders that AR101 or any future product candidates we develop will not infringe existing patents or patents that may be granted in the future. Because patent applications can take many years to issue and may be confidential for 18 months or more after filing, and because pending patent claims can be revised before issuance, there may be applications now pending of which we are unaware that may later result in issued patents that may be infringed by the manufacture, use or sale of AR101 or any future product candidates. If a patent holder believes our drug product candidate infringes on its patent, the patent holder may sue us even if we have received patent protection for our technology.

If a patent infringement suit were brought against us or any future collaborators, we or they could be forced to stop or delay the research, development, manufacturing or sales of the product or product candidate that is the subject of the suit. Defending any such claims would cause us to incur substantial expenses of financial and other resources and, if unsuccessful, we could be forced to pay substantial damages, including treble damages and attorney’s fees if we are found to have willfully infringed a third-party patent. Furthermore, we may be required to indemnify our collaborators against such claims.

We may choose to seek, or may be required to seek, a license from the third-party patent holder and would most likely be required to pay license fees or royalties or both, each of which could be substantial. These licenses may not be available on commercially reasonable terms, however, or at all. Even if we were able to obtain a license, the rights we obtain may be nonexclusive, which would provide our competitors access to the same intellectual property rights upon which we are forced to rely. Ultimately, we could be prevented from commercializing a product, or forced to redesign

it, or to cease aspects of our business operations if, as a result of actual or threatened patent infringement claims, we or our collaborators are unable to enter into licenses on acceptable terms. Even if we are successful in defending against any infringement claims, litigation is expensive and time-consuming and is likely to divert management's attention and substantial resources from our core business, which could harm our business.

We may become involved in lawsuits to protect or enforce our patents and other intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Competitors and other third parties may infringe, misappropriate or otherwise violate any patents we obtain or other intellectual property rights. To counter infringement or unauthorized use, we may be required to initiate infringement proceedings, which can be expensive and time-consuming. A court may disagree with our allegations, however, and may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the third-party technology in question. Further, such third parties could counterclaim that we infringe their intellectual property or that a patent we have asserted against them is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims challenging the validity, enforceability or scope of asserted patents are commonplace.

In addition, third parties may initiate their own legal proceedings against us to assert such challenges to our intellectual property rights. For example, we may be subject to a third-party submission of prior art to the United States Patent and Trademark Office, or USPTO, challenging the priority of an invention claimed within any patents we may obtain. Such third-party prior art submissions may also be made prior to a patent's issuance, precluding such issuance at all. We may become involved in opposition, derivation, reexamination, inter partes review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others from whom we have obtained licenses to such rights. We may also become involved in similar opposition proceedings in the European Patent Office or similar offices in other jurisdictions regarding our intellectual property rights.

The outcome of any such proceeding is generally unpredictable. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Patents may be unenforceable if someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. It is possible that prior art of which we and the patent examiner were unaware during prosecution exists, which could render any patents we obtain invalid. Moreover, it is also possible that prior art may exist that we are aware of but do not believe is relevant to patents we may obtain, but that could nevertheless be determined to render such patents invalid. An adverse result in any litigation or other proceeding to defend or enforce any patents we may obtain could put one or more of such patents at risk of being invalidated, held unenforceable, or interpreted narrowly. If a defendant were to prevail on a legal assertion of invalidity or unenforceability of any patents we obtain covering AR101 or future product candidates, we would lose at least part, and perhaps all, of any patent protection covering such product candidate, which would materially impair our competitive position.

Intellectual property litigation could cause us to spend considerable resources and would be likely to distract our personnel from their normal responsibilities.

Litigation or other legal proceedings relating to intellectual property claims, with or without merit, is unpredictable and generally expensive and time-consuming and is likely to divert significant resources from our core business, including distracting our technical and management personnel from their normal responsibilities. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities.

We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing upon or misappropriating or from successfully challenging our intellectual property rights. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

Changes in U.S. patent law 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 success is heavily dependent on intellectual property, including patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both technological and legal complexity. Therefore, obtaining and enforcing biopharmaceutical patents is costly, time consuming and inherently uncertain. Recent patent reform legislation in the United States and other countries, including the

Leahy-Smith America Invents Act, or Leahy-Smith Act, signed into law on September 16, 2011, could increase those uncertainties and costs. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications are prosecuted, redefine prior art and provide more efficient and cost-effective avenues for competitors to challenge the validity of patents. In addition, the Leahy-Smith Act has transformed the U.S. patent system into a “first-to-file” system. The first-to-file provisions, however, only became effective on March 16, 2013. Accordingly, it is not yet clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could make it more difficult to obtain patent protection for our technology and could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of any patents we obtain, all of which could harm our business, results of operations and financial condition.

The United States Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening 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 federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce any patents that we might obtain in the future.

Obtaining and maintaining our 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.

The USPTO and various foreign patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions to maintain patent applications and issued patents. In addition, periodic maintenance fees and various other governmental fees on patents and patent applications often must be paid to the USPTO and foreign patent agencies over the lifetime of the patents or for the prosecution of patent applications. While an unintentional lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance 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. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we fail to maintain the patents and patent applications covering our products or procedures, we may not be able to stop a competitor from marketing products that are the same as or similar to our products, which would have a material adverse effect on our business.

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

Filing, prosecuting and defending patents on our product candidates in all countries throughout the world would be prohibitively expensive. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The requirements for patentability differ, in varying degrees, from country to country. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patent and other intellectual property rights, especially those relating to life sciences. This could make it difficult for us to stop the infringement of any patents we obtain or the misappropriation of our other intellectual property rights. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit. Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws.

Proceedings to enforce our patent rights in foreign jurisdictions, regardless of whether successful, would result in substantial costs and divert our efforts and attention from other aspects of our business. Furthermore, while we intend to protect our intellectual property rights in our expected significant markets, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market AR101 or any future products. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate, which may have an adverse effect on our ability to successfully commercialize our products in all of our expected significant foreign markets.

If we are unable to protect the confidentiality of our trade secrets and proprietary know-how or if competitors independently develop viable competing products, our business and competitive position may be harmed.

We rely on trade secrets and confidentiality agreements to protect our proprietary know-how and other confidential information related to our development processes and other elements of our technology for which patent protection may not be available or may be difficult to obtain or enforce. Although we require all of our employees to assign their inventions to us, and endeavor to execute confidentiality agreements with all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how and other confidential information related to such technology, we cannot be certain that we have executed such agreements with all parties who may have helped to develop our intellectual property or who had access to our proprietary information, nor can we be certain that our agreements will not be breached.

Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. We cannot guarantee that our trade secrets and other proprietary and confidential information will not be disclosed or that competitors will not otherwise gain access to our trade secrets. If any of the parties to these confidentiality agreements breaches or violates the terms of such agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets as a result. Enforcing a claim that a third party illegally obtained and is using our trade secrets, like patent litigation, is expensive and time-consuming, and the outcome is unpredictable. Further, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad.

Even if we are able to adequately protect our trade secrets and proprietary information, our trade secrets could otherwise become known or could be independently discovered by our competitors. Competitors could purchase our products and attempt to replicate some or all of the competitive advantages we derive from our development efforts, willfully infringe our intellectual property rights, design around our protected technology or develop their own competitive technologies that fall outside of our intellectual property rights. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, in the absence of patent protection, we would have no right to prevent them, or those to whom they communicate, from using that technology or information to compete with us. If our trade secrets are not adequately protected so as to protect our market against competitors' products, our competitive position could be adversely affected, as could our business.

Risks Related to Our Common Stock

Our stock price may be volatile, and investors in our common stock could incur substantial losses.

The trading price of our common stock has been highly volatile and could be subject to wide fluctuations in response to various factors, including the following:

- results of, or delays in, our clinical trials;
- delays in our product development timelines;
- the number, size and type of additional clinical trials or studies that we choose to conduct or the FDA requires us to complete for AR101 prior to or following submission of our BLA and the cost and time of such trials and studies;
- regulatory approval or our receipt of a complete response letter to AR101 and our other product candidates, or limitations to specific label indications or patient populations for its use, or changes or delays in the regulatory review process;
- severe adverse events in our trials or in our competitors' trials as a result of exposure to the peanut allergen;
- therapeutic innovations or new products developed by us or our competitors;
- adverse actions taken by regulatory authorities with respect to our clinical trials, manufacturing supply chain or sales and marketing activities;
- changes or developments in laws or regulations applicable to AR101 and our other product candidates;
- any changes to our relationship with any manufacturers or suppliers;
- the success or failure of our efforts to acquire, license or develop additional product candidates;
- any intellectual property infringement actions in which we may become involved;
- announcements concerning our competitors or the pharmaceutical industry in general;
- achievement of expected product sales and profitability;
- manufacturing, supply or distribution delays or shortages;
- acquisitions or significant partnerships by us or our competitors;
- actual or anticipated fluctuations in our operating results;
- changes in financial estimates or recommendations by securities analysts;
- failure to meet financial projections that we or the investment community may provide;
- trading volume of our common stock;
- an inability to obtain additional funding;
- sales of our common stock by us, our executive officers and directors or our stockholders in the future;
- general economic and market conditions and overall fluctuations in the United States equity markets; and
- additions or departures of any of our key scientific or management personnel.

As a result of this volatility, investors may experience losses on their investment in our stock.

In addition, the stock markets in general, and the markets for pharmaceutical, biopharmaceutical and biotechnology stocks in particular, have experienced extreme volatility that may have been unrelated to the operating performance of the issuer. These broad market fluctuations may adversely affect the trading price or liquidity of our common stock. In the past, when the market price of a stock has been volatile, holders of that stock have sometimes instituted securities class action litigation against the issuer. If any of our stockholders were to bring such a lawsuit against us, we could incur substantial costs defending the lawsuit and the attention of our management would be diverted from the operation of our business, which could seriously harm our financial position. Any adverse determination in litigation could also subject us to significant liabilities.

An active market for our common stock may not be maintained

Prior to our IPO in August 2015, there had been no public market for shares of our common stock. Our stock only recently began trading on The NASDAQ Global Select Market, but we can provide no assurance that we will be able to maintain an active trading market on The NASDAQ Global Select Market or any other exchange in the future. If an active market for our common stock does not develop or is not maintained, it may be difficult for our stockholders to sell shares without depressing the market price for the shares or at all. An inactive market may also impair our ability to raise capital by selling shares and may impair our ability to acquire other businesses, applications or technologies using our shares as consideration.

If securities or industry analysts issue an adverse or misleading opinion regarding our stock, our stock price and trading volume could decline.

The trading market for our common stock is influenced by the research and reports that industry or securities analysts publish about us or our business. If any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our clinical trials and operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

As of December 31, 2016, our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates beneficially owned approximately 65% of our outstanding common stock. Therefore, these stockholders have the ability to influence us through this ownership position. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders may be able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that our stockholders may feel are in their best interest.

Provisions in our charter documents and under Delaware law could discourage a takeover that stockholders may consider favorable and may lead to entrenchment of management.

Our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could significantly reduce the value of our shares to a potential acquirer or delay or prevent changes in control or changes in our management without the consent of our board of directors. The provisions in our charter documents include the following:

- a classified board of directors with three-year staggered terms, which may delay the ability of stockholders to change the membership of a majority of our board of directors;
-

no cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;

- the exclusive right of our board of directors to elect a director to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from being able to fill vacancies on our board of directors;
- the required approval of at least 66 ⅔% of the shares entitled to vote to remove a director for cause, and the prohibition on removal of directors without cause;
- the ability of our board of directors to authorize the issuance of shares of preferred stock and to determine the price and other terms of those shares, including preferences and voting rights, without stockholder approval, which could be used to significantly dilute the ownership of a hostile acquiror;
- the ability of our board of directors to alter our bylaws without obtaining stockholder approval;

- the required approval of at least 66 2/3% of the shares entitled to vote at an election of directors to adopt, amend or repeal our bylaws or repeal the provisions of our amended and restated certificate of incorporation regarding the election and removal of directors;
- a prohibition on stockholder action by written consent, which forces stockholder action to be taken at an annual or special meeting of our stockholders;
- the requirement that a special meeting of stockholders may be called only by the chairman of the board of directors, the chief executive officer, the president or the board of directors, which may delay the ability of our stockholders to force consideration of a proposal or to take action, including the removal of directors; and
- advance notice procedures that stockholders must comply with in order to nominate candidates to our board of directors or to propose matters to be acted upon at a stockholders' meeting, which may discourage or deter a potential acquiror from conducting a solicitation of proxies to elect the acquiror's own slate of directors or otherwise attempting to obtain control of us.

In addition, these provisions would apply even if we were to receive an offer that some stockholders may consider beneficial.

We are also subject to the anti-takeover provisions contained in Section 203 of the Delaware General Corporation Law. Under Section 203, a corporation may not, in general, engage in a business combination with any holder of 15% or more of its capital stock unless the holder has held the stock for three years or, among other exceptions, the board of directors has approved the transaction.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware will be the exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is the exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a breach of fiduciary duty, any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws, or any action asserting a claim against us that is governed by the internal affairs doctrine. This provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and other employees. Alternatively, if a court were to find this provision in our 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 and financial condition.

We provide broad indemnity to our directors and officers. Claims for such indemnification may reduce our available funds to satisfy successful third-party claims against us and may reduce the amount of money available to us.

Our amended and restated certificate of incorporation and amended and restated bylaws provide that we will indemnify our directors and officers, in each case to the fullest extent permitted by Delaware law. In addition, as permitted by Section 145 of the Delaware General Corporation Law, our amended and restated bylaws and our indemnification agreements that we have entered into with our directors and officers provide that:

- We will indemnify our directors and officers for serving us in those capacities or for serving other business enterprises at our request, to the fullest extent permitted by Delaware law. Delaware law provides that a corporation may indemnify such person if such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to the best interests of the registrant and, with respect to any criminal proceeding, had no reasonable cause to believe such person's conduct was unlawful.
- We may, in our discretion, indemnify employees and agents in those circumstances where indemnification is permitted by applicable law.
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We are required to advance expenses, as incurred, to our directors and officers in connection with defending a proceeding, except that such directors or officers shall undertake to repay such advances if it is ultimately determined that such person is not entitled to indemnification.

- We will not be obligated pursuant to our amended and restated bylaws to indemnify a person with respect to proceedings initiated by that person against us or our other indemnitees, except with respect to proceedings authorized by our board of directors or brought to enforce a right to indemnification.

- The rights conferred in our amended and restated bylaws are not exclusive, and we are authorized to enter into indemnification agreements with our directors, officers, employees and agents and to obtain insurance to indemnify such persons.
    - We may not retroactively amend our amended and restated bylaw provisions to reduce our indemnification obligations to directors, officers, employees and agents.

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

Under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, if a corporation undergoes an "ownership change," generally defined as a greater than 50 percentage point change (by value) in its equity ownership over a rolling three-year period, the corporation's ability to use its pre-change net operating loss, or NOL, carryforwards to offset its post-change taxable income may be limited. Limitations may also apply to the utilization of other pre-change tax attributes as a result of an ownership change. As of December 31, 2016, we had generated NOL carryforwards for federal income tax purposes of $81.0 million and for state income tax purposes of $12.0 million. These federal and state NOL carryforwards will begin to expire in 2031, if not utilized. As described above, our ability to utilize NOL carryforwards or other tax attributes, such as research tax credits, in any taxable year may be limited if we have experienced an ownership change under Section 382 of the Code. Following the issuance of the Series B convertible preferred stock in January and February 2015, we performed a preliminary Section 382 analysis and believe that we experienced multiple ownership changes under Section 382 of the Code prior to June 30, 2015 and, as a result, such federal and state NOL carryforwards and our tax credits are subject to limitation. In addition, we may have experienced ownership changes in connection with our IPO or the equity investment by Nestle Health Science in November 2016, and may experience ownership changes as a result of future changes in our stock ownership, some of which changes may be outside our control. As a result, if we earn net taxable income, our ability to use our pre-change NOL carryforwards to offset post-change taxable income may be subject to limitations. For these reasons, we may not be able to utilize a material portion of our NOL carryforwards and other tax attributes, which could adversely affect our future cash flows.

We do not currently intend to pay dividends on our common stock, and, consequently, our stockholders' ability to achieve a return on their investment will depend on appreciation in the price of our common stock.

We do not currently intend to pay any cash dividends on our common stock for the foreseeable future. We currently intend to invest our future earnings, if any, to fund our growth. Since we do not intend to pay dividends, our stockholders' ability to receive a return on their investment in our common stock will depend on any future appreciation in the market value of our common stock. There is no guarantee that our common stock will appreciate or even maintain the price at which our holders have purchased it.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

In March 2015, we entered into a lease for our corporate headquarters in Brisbane, California for 11,665 square feet of office space. Upon the commencement of the new lease in May 2015, we ceased use of our previous corporate

headquarters. In August 2015, we entered into an amendment to the Brisbane, California lease. Pursuant to the amendment, we leased an additional 26,355 square feet of office space. The term for the new space is 72 months from the delivery of the premises to us, which took place December 2015. In addition, the term of the existing office space has been extended so that it is coterminous with the new space. In addition, we lease approximately 20,000 square feet of manufacturing space in Clearwater, Florida pursuant to a lease that expires in 2025. We believe that our existing facilities and other available properties will be sufficient for our needs for the foreseeable future.

For additional information, see Contractual Commitments and Other Obligations in Part II, Item 7 of this Annual Report on Form 10-K.

Item 3. Legal Proceedings.

We are currently not party to any material legal proceedings; however, we may from time to time be involved in various legal proceedings incident to the ordinary course of our business.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

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

Market Information

Our common stock has been listed on The NASDAQ Global Select Market under the symbol "AIMT" since our initial public offering, or IPO, of our common stock on August 6, 2015. Prior to that time, there was no public market for our common stock. The following table sets forth for the indicated periods the high and low intra-day sales prices per share for our common stock on The NASDAQ Global Select Market:

	2016	
	High	Low
First quarter	$19.00	$12.43
Second quarter	15.88	10.57
Third quarter	17.23	9.77
Fourth quarter	27.31	14.48

	2015	
	High	Low
Third quarter (beginning August 6, 2015)	$28.33	$17.50
Fourth quarter	22.94	14.77

Holders of Record

On March 10, 2017, there were approximately 21 stockholders of record of our common stock and the closing price of our common stock was $22.19 per share as reported by The NASDAQ Global Select Market. Since many of our shares of common stock are held by brokers and other institutions on behalf of stockholders, we are unable to estimate the total number of stockholders represented by these record holders.

Dividend Policy

We have never declared or paid cash dividends on our capital stock. We intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. In addition, the Securities Purchase Agreement we entered into with Nestle Health Science US Holdings, Inc. in November 2016, contractually prevents us from using any of the proceeds from the sale and issuance of the shares of our common stock as a cash dividend or distribution until the second anniversary of the closing date. Any future determination related to dividend policy will be made at the discretion of our board of directors.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

Sales of Unregistered Securities

None.

Use of Proceeds from Initial Public Offering of Common Stock

Shares of our common stock began trading on The NASDAQ Global Select Market on August 5, 2015. The shares were registered under the Securities Act, as amended, pursuant to our registration statement on Form S-1 (Registration No. 333-205501) relating to our IPO of common stock, which became effective on August 5, 2015.

There has been no material change in the planned use of proceeds from our IPO as described in our prospectus dated August 5, 2015, filed with the SEC pursuant to Rule 424(b)(4) under the Securities Act, as amended.

Stock Performance Graph

The following graph illustrates a comparison of the total cumulative stockholder return on our common stock since August 6, 2015, which is the date our common stock first began trading on The NASDAQ Global Select Market, to three indices: the NASDAQ Composite Index, the NASDAQ Biotechnology Index and the NASDAQ Pharmaceutical Index. The stockholder return shown in the graph below is not necessarily indicative of future performance, and we do not make or endorse any predictions as to future stockholder returns. This graph shall not be deemed "soliciting material" or be deemed "filed" for purposes of Section 18 of the Exchange Act, or otherwise subject to the liabilities under that Section, and shall not be deemed to be incorporated by reference into any of our filings under the Securities Act, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.

Item 6. Selected Financial Data.

The following selected financial data are derived from the consolidated financial statements. The data presented below should be read in conjunction with the consolidated financial statements of the Company, the notes to the consolidated financial statements, and "Management's Discussion and Analysis of Financial Condition and Results of Operations" included elsewhere in this Annual Report on Form 10-K.

	Year Ended December 31,			
	2016	2015	2014	2013
	(In thousands)			
Operating expenses				
Research and development	$54,642	$19,816	$8,181	$3,495
General and administrative	26,885	16,181	2,951	1,263
Total operating expenses	81,527	35,997	11,132	4,758
Loss from operations	(81,527)	(35,997)	(11,132)	(4,758)
Interest income, net	703	181	12	(67)
Net Loss	$(80,824)	$(35,816)	$(11,120)	$(4,825)
Net loss per common share, basic and diluted	$(1.89)	$(1.88)	$(3.80)	$(1.65)
Weighted average shares used in computing net loss per share, basic and diluted	42,751	19,041	2,929	2,927

	Year Ended December 31,			
	2016	2015	2014	2013
	(In thousands)			
Balance Sheet Data:				
Cash and cash equivalents	$124,010	$76,677	$2,269	$11,951
Working capital	240,230	192,359	571	11,552
Total assets	298,789	212,361	2,531	12,156
Accumulated deficit	(134,157)	(53,333)	(17,517)	(6,397)
Total stockholders' equity	285,972	206,251	671	11,637

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 in conjunction with our audited 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 statements of our plans, objectives, expectations and intentions. 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 discussed in the section of this Annual Report of on Form 10-K titled "Risk Factors." Except as may be required by law, we assume no obligation to update these forward-looking statements or the reasons that results could differ from these forward-looking statements.

Overview

We are a clinical-stage biopharmaceutical company advancing a new therapeutic approach, including the development of proprietary product candidates, for the treatment of peanut and other food allergies. It is estimated that over 30 million people in the United States and Europe have a food allergy, with peanut allergy being the most prevalent and most commonly associated with severe outcomes and life-threatening events. There are currently no approved medical therapies to cure food allergies or prevent their symptoms. Patients with food allergies are typically counseled to practice strict dietary avoidance. When accidental exposure to food allergens invokes a serious allergic reaction, rescue therapies, such as antihistamines or injectable epinephrine, are the only recourse available. Our therapeutic approach, which we refer to as Characterized Oral Desensitization ImmunoTherapy, or CODIT™, is designed to desensitize patients to food allergens and thereby reduce the risk of having an allergic reaction upon accidental exposure, or reduce symptom severity should an allergic reaction occur. CODIT is intended to reduce meaningfully the burden and anxiety experienced by food-allergic patients and their families.

Our lead CODIT product candidate, AR101, is an investigational biologic for the treatment of patients with peanut allergy, which affects approximately three million patients in the United States and three million patients in Europe. AR101 has received Fast Track and Breakthrough Therapy Designations for the treatment of patients 4-17 years from the United States Food and Drug Administration, or FDA. Our initial target patient population is in children and adolescents in the 4-17 age group, which we estimate will reach approximately 1.6 million patients in the United States alone by 2018. We have completed a double-blind placebo-controlled Phase 2 trial of AR101 in 55 patients ages 4-21 years, have analyzed longer-term safety and efficacy data from our ongoing open-label Phase 2 trial and have received feedback from regulatory authorities, including the FDA and the European Medicines Agency, or EMA, providing guidance on our Phase 3 program. In late 2015, we initiated a Phase 3 registration trial of AR101 in the United States, Canada and Europe, which we refer to as the PALISADE (Peanut Allergy Oral Immunotherapy Study of AR101 for Desensitization in Children and Adults) trial. We completed global enrollment of 554 patients ages 4-49 in November 2016 and anticipate completing the PALISADE trial around year-end 2017. We have begun to enroll eligible patients who have completed PALISADE into a related open-label Phase 3 roll-over trial, which we refer to as the ARC004 trial. We expect to begin enrolling a real-world experience trial of AR101 in the United States and Canada in patients ages 4-17 in the second quarter of 2017, which we refer to as the RAMSES (Real-World AR101 Market-Supporting Experience Study in Peanut Allergic Children Ages 4-17 Years) trial. In addition, we expect to initiate a European trial in the middle of 2017 designed with a higher efficacy bar in the same age group, which we refer to as the ARTEMIS (AR101 Trial in Europe Measuring oral Immunotherapy Success) trial. Based on discussions with the FDA in the beginning of 2017, we anticipate that the safety database for a Biologics License Application, or BLA, will need to include data from at least 600 patients ages 4-17 treated with AR101 at the target maintenance dose of 300 mg per day. We expect to meet this requirement with patients from the PALISADE, ARC004 and RAMSES trials. In Europe, we expect that data from the PALISADE, ARC004 and ARTEMIS trials will form the basis for a Marketing Authorization Application, or MAA, filing with the European Medicines Agency, or EMA. We expect to have topline data from our PALISADE trial around year-end 2017 and intend to file a BLA in the United States and an MAA in the European Union in late 2018.

We maintain worldwide commercial rights to all of our product candidates, including AR101 and, if approved, currently intend to commercialize in the United States and Europe with our own specialty sales force calling on allergists in the United States and allergy-focused clinicians in major European markets.

Since commencing our operations in 2011, substantially all of our efforts have been focused on research, development and the advancement of our lead CODIT product candidate, AR101. We have not generated any revenue from product sales and, as a result, we have incurred significant losses. We incurred net losses of $80.8 million, $35.8 million, and $11.1 million for the years ended December 31, 2106, 2015, and 2014, respectively. As of December 31, 2016 our accumulated deficit was $134.2 million. We expect to continue to incur losses for the foreseeable future, and we anticipate these losses will increase as we continue our development of, seek regulatory approval for, and begin to commercialize AR101, and as we develop other product candidates.

We do not expect to generate revenue from product sales unless and until we successfully complete development of, obtain regulatory approval for, and begin to commercialize one or more of our product candidates, which we expect will take a number of years and is subject to significant uncertainty. Accordingly, we anticipate that we will need to raise additional capital to fund our future operations. Until such time that we can generate substantial revenue from product sales, if ever, we expect to finance our operating activities through a combination of equity offerings and debt financings and we may seek to raise additional capital through strategic collaborations. However, we may be unable to raise additional funds or enter into such arrangements when needed on favorable terms, or at all, which would have a negative impact on our financial condition and could force us to delay, limit, reduce or terminate our development programs or commercialization efforts or grant to others rights to develop or market product candidates that we would otherwise prefer to develop and market ourselves. Failure to receive additional funding could cause us to cease operations, in part or in full. Furthermore, even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital due to favorable market conditions or strategic considerations.

We currently utilize contract manufacturers for all of our manufacturing activities. In June 2015, we entered into a lease for a manufacturing facility in Clearwater, Florida. We anticipate that this manufacturing facility will be operational by the end of 2017. We plan to continue to rely on the contract manufacturer that is located at the same site to manage the operations of this new manufacturing facility. Additionally, we currently utilized specialized clinical vendors, clinical trial sites, consultants, and clinical research organizations, or CROs, to ensure the proper and timely conduct of our clinical trials, and we do not yet have a sales organization. We expect to significantly increase our investment in costs relating to our manufacturing process and sales organization as we prepare for the filing of a BLA with the FDA and a MAA with the EMA and prepare for a possible commercial launch of AR101.

Recent Developments

Equity Investment and Strategic Collaboration

On November 3, 2016, we entered into a securities purchase agreement (the “Purchase Agreement”) with Nestle Health Science US Holdings, Inc. (“Nestle Health Science”), pursuant to which we issued and sold 7,552,084 shares (“the Shares”) of our common stock, par value $0.0001 to Nestle Health Science in a private placement at a price of $19.20 per share or aggregate cash purchase price of $145.0 million. The Shares represented 15.1% of our outstanding common stock after giving effect to the issuance of the shares upon closing. In connection with the closing of the sale and issuance of the Shares on November 23, 2016, we entered into a Registration Rights Agreement, and Standstill Agreement with Nestle Health Science.

In connection with the Purchase Agreement, on November 3, 2016, we entered into a Strategic Collaboration Agreement (the “Strategic Collaboration Agreement”) with Nestec, Ltd., a limited company organized and existing under the laws of Switzerland (“Nestec”). Nestec and Nestle Health Science are affiliates of Swiss food and wellness company, Nestlé S.A. Pursuant to the Strategic Collaboration Agreement, we and Nestec (through itself and one or more affiliated entities) agreed to collaborate with one another in connection with the development of our products, including by (i) sharing information relating to our activities directed towards the development of our products for the treatment of allergies to one or more particular types of food (the “Development Programs”) and (ii) providing us access to Nestec’s scientific, clinical, regulatory and commercial expertise relevant to such Development Programs. The Strategic Collaboration Agreement became effective upon the closing of the equity investment. We evaluated the Equity Purchase Agreement and Strategic Collaboration Agreement and determined that the equity purchase by Nestle Health Science was at fair value, and therefore, we accounted for the equity component under the Equity Purchase Agreement separately from the Strategic Collaboration Agreement. The collaboration is not deemed to be a revenue generating transaction and no accounting was required.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with generally accepted accounting principles, or GAAP, in the United States. The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, as well as the reported revenue generated and 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. Our significant accounting policies are more fully described in Note 2 of Notes to Consolidated Financial Statements in Part II, Item 8 of this Annual Report on Form 10-K.

Accrued Research and Development Costs

We record expenses for our research and development activities conducted by third-party service providers, which include the conduct of pre-clinical studies and clinical trials and contract manufacturing activities, based upon the estimated amount of services provided and work completed but not yet invoiced and in accordance with agreements established with these third-party service

providers. We include these costs in accrued liabilities in the consolidated balance sheets and within research and development expenses in the consolidated statements of operations and comprehensive loss. These costs are a significant component of our research and development expenses.

We estimate the amount of work completed 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. We make significant judgments and estimates in determining the accrued balance in each reporting period. 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 clinical research organizations and other third-party service providers. To date, there have been no material differences from our accrued expenses to actual expenses.

Stock-Based Compensation

We recognize compensation costs related to stock options granted to employees and directors based on the estimated fair value of the awards on the date of grant, net of estimated forfeitures. We estimate the grant date fair value using the Black-Scholes option-pricing model. The grant date fair value of the stock-based awards is generally recognized on a straight-line basis over the requisite service period, which is generally the vesting period of the respective awards.

We recorded stock-based compensation expense of $12.6 million, $6.2 million and $0.1 million for the years ended December 31, 2016, 2015 and 2014, respectively.

Prior to our IPO, the fair value of our shares of common stock underlying the stock options was the responsibility of and determined by our Board of Directors, or the Board. Because there was no public market for our common stock, the Board determined the fair value of common stock at the time of grant of the option by considering a number of objective and subjective factors, including independent third-party valuations of our common stock, sales of convertible preferred stock to unrelated third parties, operating and financial performance, the lack of liquidity of our capital stock, and general and industry specific economic outlook, amongst other factors. Following our IPO, the market traded price of the shares of common stock underlying the stock options is the closing price of our stock as reported on The NASDAQ Global Select Market on the grant date.

In determining the fair value of the stock-based awards used to calculate stock-based compensation expense, we use the Black-Scholes option-pricing model and assumptions discussed below. Some of these inputs are subjective and require judgment to determine.

- Expected Term. The expected term of stock options represents the weighted average period the stock options are expected to be outstanding. We have opted to use the simplified method for estimating the expected term as provided by the Securities and Exchange Commission Staff Accounting Bulletin, or SAB, 110 as our options grants are considered “plain vanilla”. The simplified method calculates the expected term as the average time-to-vesting and the contractual life of the options. We plan to continue to use the simplified method under SAB 110 until we have sufficient exercise history as a publicly traded company.
- Expected Volatility. The expected stock price volatility assumption was determined by examining the historical volatilities of a group of industry peers, as we have limited trading history for our common stock. Industry peers consist of several public companies in the biopharmaceutical industry with comparable characteristics including enterprise value, risk profiles and position within the industry. We intend to continue to consistently apply this process using the same or similar public companies until a sufficient amount of historical information regarding the volatility of our own common stock share price becomes available, or unless circumstances change such that the identified companies are no longer similar to us, in which case, more suitable companies whose share prices are

publicly available would be utilized in the calculation.

- Risk-Free Interest Rate. The risk-free interest rate is based on the implied yield available on U.S. Treasury zero-coupon issues in effect at the time of grant for periods corresponding with the expected term of the option.
- Expected Dividend Yield. We have never paid dividends on our common stock and have no plans to pay dividends on our common stock. Therefore, we used an expected dividend yield of zero for all years presented.

The weighted-average assumptions used to estimate the fair value of stock options using the Black-Scholes option valuation model and the resulting weighted average grant date fair value of stock options granted were as follows:

	Year Ended December 31,		
	2016	2015	2014
Expected volatility	74.46%	74.14%	79.62%
Risk-free interest rate	1.71 %	1.73 %	1.51 %
Expected dividend yield	—	—	—
Expected term (in years)	6.03	5.99	4.65
Weighted average grant date fair value	$10.53	$6.11	$0.09

In addition to the Black-Scholes assumptions, we estimate our forfeiture rate based on an analysis of our actual forfeitures and will continue to evaluate the adequacy of the forfeiture rate based on actual forfeiture experience, analysis of employee turnover behavior and other factors. The impact from any forfeiture rate adjustment would be recognized in full in the period of adjustment, and if the actual number of future forfeitures differs from our estimates, we might be required to record adjustments to stock-based compensation in future periods. We will continue to use judgment in evaluating the expected volatility, expected terms and forfeiture rates utilized for our stock-based compensation expense calculations on a prospective basis.

As of December 31, 2016, we had $27.3 million of unrecognized compensation expense related to unvested stock options, which is expected to be recognized over an estimated weighted-average period of 2.72 years. For stock option awards subject to ratable vesting, we recognize compensation cost on a straight-line basis over the service period for the entire award. In future periods, our stock-based compensation expense is expected to increase as a result of recognizing our existing unrecognized stock-based compensation for awards that will vest and as we issue additional stock-based awards to attract and retain our employees.

Income Taxes

We recognize deferred income taxes for temporary differences between the basis of assets and liabilities for financial statement and income tax purposes. We periodically evaluate the positive and negative evidence bearing upon realizability of our deferred tax assets. Based upon the weight of available evidence, which includes our historical operating performance, reported cumulative net losses since inception and difficulty in accurately forecasting our future results, we maintained a full valuation allowance on the net deferred tax assets. We intend to maintain a full valuation allowance on the federal and state deferred tax assets until sufficient positive evidence exists to support reversal of the valuation allowance.

As of December 31, 2016, we had generated net operating loss, or NOL, carryforwards for federal income tax purposes of $81.0 million and for California income tax purposes of $12.0 million. These federal and state NOL carryforwards will begin to expire in 2031, if not utilized. Our ability to utilize NOL carryforwards or other tax attributes, such as research tax credits, in any taxable year may be limited if we have experienced an ownership change under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code. Following issuance of the Series B convertible preferred stock in January and February 2015, we performed a preliminary Section 382 analysis and believe that we experienced multiple ownership changes prior to June 30, 2015, and, as a result, such federal and state NOL carryforwards and our tax credits are subject to limitation. We have not performed a Section 382 analysis to evaluate whether or not we experienced an ownership change as a result of either our August 2015 IPO or the November 2016 equity investment by Nestle Health Science.

We record unrecognized tax benefits as liabilities and adjust these liabilities when our judgment changes as a result of the evaluation of new information not previously available. Because of the complexity of some of these uncertainties, the ultimate resolution may result in a payment that is materially different from our current estimate of the unrecognized tax benefit liabilities. These differences will be reflected as increases or decreases to deferred tax assets offset by a change to valuation allowance in the period in which new information is available.

Tax benefits from uncertain tax positions are recognized when it is more likely than not that the position will be sustained upon examination, including resolutions of any related appeals or litigation processes, based on technical merits. The amount recognized is measured as the largest amount of tax benefit that is greater than 50% likely of being realized upon effective settlement.

Recently Issued Accounting Pronouncements Not Yet Adopted

In November 2016, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, 2016-18, Statement of Cash Flows – Restricted Cash (Topic 230), which establishes that the statement of cash flows will show the changes in cash, cash equivalents and amounts generally described as restricted cash. As a result, entities will no longer have to determine how to classify transfers to and from restricted cash within the statement of cash flows. An entity will be required to reconcile the total cash, cash equivalents and amounts generally described as restricted cash on the statement of cash flows to the amounts in the balance sheet, and disclose the nature of any restrictions on its cash, cash equivalents or amounts generally described as restricted cash. This guidance is effective for fiscal years, and interim periods within those years, beginning after December 31, 2017, and early adoption is permitted. We have not yet adopted ASU 2016-18, but we do not expect the standard to have a material impact on our financial statements and related disclosures.

In October 2016, the FASB, issued ASU, 2016-16, Income Taxes (Topic 740): Intra-Entity Transfers Other Than Inventory, which requires companies to recognize the income tax consequences of an intra-entity transfer of an asset other than inventory. This guidance will be effective for us in the first quarter of 2018, with the option to adopt it in the first quarter of 2017. We currently anticipate adopting the new standard effective January 1, 2018, and do not expect the standard to have a material impact on our financial statements and related disclosures.

In August 2016, the FASB issued ASU 2016-15, Statement of Cash Flows (Topic 230): Classification of Certain Cash Receipts and Cash Payments, which will make eight targeted changes to how cash receipts and cash payments are presented and classified in the statement of cash flows. ASU 2016-15 is effective for fiscal years beginning after December 15, 2017. ASU 2016-15 will require adoption on a retrospective basis. Early adoption is permitted. We are currently evaluating the impact that the adoption of ASU 2016-15 will have on our financial statements and related disclosures.

In June 2016, the FASB issued ASU 2016-13, Financial Instruments — Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments, which requires measurement and recognition of expected credit losses for financial assets held. ASU 2016-13 modifies the other-than-temporary impairment model for available-for-sale debt securities and requires an estimate of expected credit losses when the fair value is below the amortized cost of the asset. ASU 2016-13 is effective for fiscal years beginning after December 15, 2019 and interim periods within those fiscal years. Early adoption is permitted. We are currently evaluating the impact that the adoption of ASU 2016-13 will have on our financial statements and related disclosures.

In March 2016, the FASB, issued ASU 2016-09, Compensation—Stock Compensation (Topic 718) Improvements to Employee Share-Based Payment Accounting, which simplifies several aspects of accounting for share-based payment transactions including the income tax consequences, classification of awards as either equity or liabilities, classification on the statement of cash flows and accounting for forfeitures. The new standard is effective for fiscal years beginning after December 15, 2016, and interim periods within those fiscal years with early adoption permitted. We do not expect the adoption of this new standard to have a material impact on our financial statements and related disclosures.

In February 2016, the FASB, issued ASU, No. 2016-02, Leases (Topic 842), which requires lessees to apply a dual approach, classifying leases as either finance or operating leases based on the principle of whether or not the lease is effectively a financed purchase by the lessee. This classification will determine whether lease expense is recognized based on an effective interest method or on a straight-line basis over the term of the lease. A lessee is also required to record a right-of-use asset and a lease liability for all leases with a term of greater than 12 months regardless of their classification. Leases with a term of 12 months or less will be accounted for similar to existing guidance for operating leases. The standard is effective for interim and annual periods beginning after December 15, 2018, with early adoption permitted. We are currently in the process of evaluating the impact the adoption of this new standard will have on our financial statements and related disclosures; however, since we are lessee to certain leases for property

whose terms exceed twelve months, we expect to report assets and liabilities related to these leases on our financial statements that have not been previously reported, once we adopt ASU 2016-02.

Components of Results of Operations

Research and Development Expenses

The largest component of our total operating expenses has historically been our investment in research and development activities. Research and development expenses consist primarily of external-related expenses, employee-related expenses, stock-based compensation expense, and facilities and other costs, which include the following:

- External-related expenses include costs incurred to conduct research, such as the discovery and development of our product candidates; costs related to the production of clinical supplies, including fees paid to contract manufacturers; fees paid to consultants and vendors, including clinical research organizations in conjunction with implementing and monitoring our clinical trials and acquiring and evaluating clinical trial data, including all related fees, such as for investigator grants, patient screening fees, laboratory work and statistical compilation and analysis; costs for scientific conferences and meetings; and costs related to compliance with drug development regulatory requirements.
- Employee-related costs include salaries, bonuses, severance and benefits for personnel in our research and development functions.
- Stock-based compensation expense is expense associated with our equity plans for awards to personnel in our research and development functions.
- Facilities and other costs include facilities-related rent, depreciation and other allocable expenses, which include general and administrative support functions and general supplies for our research and development activities.

We recognize all research and development expenses as they are incurred. Clinical trial, contract manufacturing and other development costs incurred by third parties are expensed as the contracted work is performed.

General and Administrative Expenses

General and administrative expenses include employee-related costs, stock-based compensation expense, external professional services expenses, and facilities and other costs. Employee-related costs include salaries, bonuses, severance and benefits for personnel in our general and administrative functions. Stock-based compensation expense is expense associated with our equity plans for awards to personnel in our general and administrative functions. External professional services expenses consist of legal, accounting, and audit services and other consulting fees. Facilities and other costs consist of facilities-related rent, depreciation, and other allocable expenses, which include general and administrative support functions, general supplies and insurance costs.

Results of Operations

Comparison of the years ended December 31, 2016 and 2015

	Year Ended December 31,				
	2016	2015	$ Change	% Change	
	(In thousands)				
Operating expenses:					
Research and development	$54,642	$19,816	$34,826	176	%
General and administrative	26,885	16,181	10,704	66	%
Total operating expenses	81,527	35,997	45,530	126	%
Loss from operations	(81,527)	(35,997)	(45,530)	126	%
Interest income, net	703	181	522	288	%

Net loss	$(80,824)	$(35,816)	$(45,008)	126 %

Research and Development Expenses

The following table summarizes our research and development expenses incurred during the years ended December 31, 2016 and 2015:

	Year Ended December 31,				
	2016	2015	$ Change	% Change	
	(In thousands)				
External clinical-related expenses	$37,133	$12,096	$25,037	207	%
Employee-related costs	10,342	4,394	5,948	135	%
Stock-based compensation expense	4,838	2,522	2,316	92	%
Facilities and other costs	2,329	804	1,525	190	%
Total research and development	$54,642	$19,816	$34,826	176	%

Research and development expenses increased by $34.8 million for the year ended December 31, 2016 compared to the year ended December 31, 2015, primarily due to increased external clinical-related expenses, employee-related costs, stock-based compensation expense and facilities and other costs. External clinical-related costs increased primarily due to activities related to enrolling patients in and conducting PALISADE, which was initiated in late 2015, and contract manufacturing costs of AR101 for clinical trials. Employee-related costs increased primarily due to increased headcount to support continued development of AR101. Stock-based compensation expense increased primarily due to increased headcount, higher valuation of stock options granted and expense related to the acceleration of vesting of certain former executives' stock options. Facilities and other costs increased primarily due to increased rent expense from our new facility leases and other allocable costs due to increased headcount.

We expect research and development expenses to continue to increase as PALISADE continues and patients move into ARC004, the open-label follow-on study to PALISADE, we initiate and enroll new AR101 studies, RAMSES and ARTEMIS, and develop additional CODIT product candidates.

General and Administrative Expenses

The following table summarizes our general and administrative expenses incurred during the years ended December 31, 2016 and 2015:

	Year Ended December 31,				
	2016	2015	$ Change	% Change	
	(In thousands)				
Employee-related costs	$8,406	$3,901	$4,505	115	%
Stock-based compensation expense	7,803	3,635	4,168	115	%
External professional services	8,542	6,567	1,975	30	%
Facilities and other costs	2,134	2,078	56	3	%
Total general and administrative	$26,885	$16,181	$10,704	66	%

General and administrative expenses increased by $10.7 million for the year ended December 31, 2016 compared to the year ended December 31, 2015, primarily due to increased employee-related costs, stock-based compensation expense, and external professional services. Employee-related costs increased primarily due to increased headcount for additional administrative support associated with being a publicly traded company following our initial public offering, or IPO, in August 2015. Stock-based compensation expense increased primarily due to increased headcount, higher valuation of stock options granted, and the modification of certain former executives' stock options. External professional services increased primarily due to consulting services, including for commercial planning and support for AR101.

We expect our general and administrative expenses to continue to increase as we continue to build our infrastructure as a publicly traded company, including the hiring of additional personnel, and incur expenses related to commercial planning for AR101.

Interest Income, net

Interest income, net, increased by $0.5 million for the year ended December 31, 2016 compared to the year ended December 31, 2015 primarily due to higher average cash and investment balances during the period.

Comparison of the years ended December 31, 2015 and 2014

	Year Ended December 31,			
	2015	2014	$ Change	% Change
	(In thousands)			
Operating expenses:				
Research and development	$19,816	$8,181	$11,635	142 %
General and administrative	16,181	2,951	13,230	448 %
Total operating expenses	35,997	11,132	24,865	223 %
Loss from operations	(35,997)	(11,132)	(24,865)	223 %
Interest income, net	181	12	169	*
Net loss	$(35,816)	$(11,120)	$(24,696)	222 %

*Percentage not meaningful

Research and Development Expenses

The following table summarizes our research and development expenses incurred during the years ended December 31, 2015 and 2014:

	Year Ended December 31,			
	2015	2014	$ Change	% Change
	(In thousands)			
External clinical-related expenses	$12,096	$6,399	$5,697	89 %
Employee-related costs	4,394	1,536	2,858	186 %
Stock-based compensation expense	2,522	23	2,499	*
Facilities and other costs	804	223	581	261 %
Total research and development	$19,816	$8,181	$11,635	142 %

*Percentage not meaningful

Research and development expenses increased by $11.6 million for the year ended December 31, 2015, compared to the year ended December 31, 2014, which was primarily due to increases in external clinical-related expense, employee-related costs, and stock-based compensation expense. The increase in employee-related costs and stock-based compensation expense was primarily due to increased headcount to support continued AR101 development. External clinical-related expenses increased due to our Phase 2 clinical trial and the initiation of PALISADE, in 2015, and as a result of expenses associated with the continued development of AR101.

General and Administrative Expenses

The following table summarizes our general and administrative expenses incurred during the years ended December 31, 2015 and 2014:

	Year Ended December 31,				
	2015	2014	$ Change	% Change	
	(In thousands)				
Employee-related costs	$3,901	$1,662	$2,239	135	%
Stock-based compensation expense	3,635	54	3,581	*	
External professional services	6,567	786	5,781	735	%
Facilities and other costs	2,078	449	1,629	363	%
Total general and administrative	$16,181	$2,951	$13,230	448	%

*Percentage not meaningful

General and administrative expenses increased by $13.2 million for the year ended December 31, 2015, compared to the year ended December 31, 2014, which was primarily due to increases in employee-related costs, stock-based compensation expense, external professional services and facility and other costs. The increases in employee-related costs and stock-based compensation expense were primarily due to increased headcount for additional administrative and executive personnel to support being a public company. Stock-based compensation expense also increased due to a charge of $1.4 million related to the acceleration of certain former executives' stock options. External professional services increased primarily due to higher costs incurred for financial consulting and market research to inform our commercial strategy and support growth. Facility and other costs increased primarily as a result of our new leases.

Interest Income, net

Interest income, net, increased by $0.2 million for the year ended December 31, 2015 compared to the year ended December 31, 2014. The increase was due to higher cash, cash equivalents and investment balances resulting from the proceeds of our IPO in August 2015, and from the issuance of Series B convertible preferred stock in January and February 2015.

Liquidity and Capital Resources

As of December 31, 2016, we had cash, cash equivalents and investments of $282.5 million. We believe that our existing capital resources will be sufficient to fund our planned operations for at least the next 12 months and through regulatory submissions for AR101.

In January and February 2015, we received net proceeds of $79.8 million from the sale of our Series B convertible preferred stock, of which $12.9 million was used to repurchase outstanding shares of our Series A convertible preferred stock.

In August 2015, we completed our IPO and issued 11,499,999 shares of our common stock, par value $0.0001 per share, including the exercise in full of the underwriter's option to purchase additional shares, at an initial offering price to the public of $16.00 per share. We received net proceeds from the IPO of $168.1 million, after deducting underwriting discounts and commissions of $12.9 million and offering costs of $3.0 million. Prior to our IPO, our operations were financed primarily by net proceeds from the sale and issuance of convertible preferred stock.

In November 2016, we and Nestle Health Science entered into the Purchase Agreement, pursuant to which we issued and sold 7,552,084 shares of our common stock, par value $0.0001 per share, to Nestle Health Science for an aggregate cash purchase price of $145.0 million.

We do not expect to generate revenue from product sales unless and until we successfully complete development of, obtain regulatory approval for, and begin to commercialize one or more of our product candidates, which we expect will take a number of years and is subject to significant uncertainty. Accordingly, we anticipate that we will need to raise additional capital to fund our future operations. Until such time that we can generate substantial revenue from product sales, if ever, we expect to finance our operating activities through a combination of equity offerings and debt financings and we may seek to raise additional capital through strategic collaborations. However, we may be unable to raise additional funds or enter into such arrangements when needed on favorable terms, or at all, which would have a negative impact on our financial condition and could force us to delay, limit, reduce or terminate our development programs or commercialization efforts or grant to others rights to develop or market product candidates that we would otherwise prefer to develop and market ourselves. Failure to receive additional funding could cause us to cease operations, in part or in full. Furthermore, even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital due to favorable market conditions or strategic considerations.

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

- the time and cost necessary to complete our PALISADE trial and the related roll-over study, ARC004, as well as the time and costs associated with the other planned development activities for AR101 including the initiation and operation of RAMSES, ARTEMIS and ARC008;
    - the number, size and type of additional clinical trials or studies that we choose to initiate or the FDA or a foreign regulatory authority requires us to complete for AR101 prior to or following submission of our Biologics License Application, or BLA, or other marketing approval applications, as well as the cost and time of such trials and studies;
- the time and cost necessary to supply clinical trial materials for our clinical trials and develop a commercial-scale manufacturing process for AR101;
- the time and cost associated with clinical trials and pre-clinical development of other product candidates;

- our ability to obtain regulatory approval for and subsequently commercialize AR101 or any other product candidates we develop;
- sales and marketing costs associated with AR101, if approved, including the cost and timing of developing our sales and marketing capabilities;
- the amount of sales and other revenue from AR101, if approved;
- our ability to achieve sufficient market acceptance, coverage and reimbursement from third-party payors and adequate market share for our product candidates;
- the time and cost associated with designing and implementing quality systems for our product candidates in the United States and Europe;
- the cash requirements of any future acquisitions or discovery of product candidates;
- the time and cost necessary to respond to technological and market developments;
- our ability to attract, hire and retain qualified personnel; and
- our ability to obtain and maintain intellectual property protection for AR101 or any future product candidate and the associated costs of such activities, including for filing, prosecuting, defending and enforcing any patents for AR101 or any future product candidate.

Additional funds may not be available when we need them, on terms that are acceptable to us, or at all. If adequate funds are not available to us on a timely basis, we may be required to delay, limit, reduce or terminate:

- clinical trials or other development activities for AR101 or any future product candidate;
- our research and development activities; or
- our establishment of sales and marketing capabilities or other activities that may be necessary to commercialize AR101 or any future product candidate.

Cash Flows

Comparison of the years ended December 31, 2016 and 2015

	Year Ended December 31,		
	2016	2015	Change
	(In thousands)		
Net cash provided by (used in):			
Operating activities	$(56,614)	$(35,690)	$(20,924)
Investing activities	(43,896)	(125,229)	81,333
Financing activities	147,843	235,327	(87,484)
Net change in cash and cash equivalents	$47,333	$74,408	$(27,075)

Net Cash Used In Operating Activities

Net cash used in operating activities was $56.6 million for the year ended December 31, 2016, an increase of $20.9 million from $35.7 million for the year ended December 31, 2015. This increase was primarily due to higher net loss from operations resulting from increased research and development and general and administrative expenses.

Net Cash Used In Investing Activities

Cash used in investing activities was $43.9 million for the year ended December 31, 2016, a decrease of $81.3 million from $125.2 million for the year ended December 31, 2015. The decrease was primarily due to the maturities of various investments we had made after our IPO, which partially offset purchases of new investments in 2016, including those made in conjunction with the proceeds received in the NHSc US investment of $145.0 million.

Additionally, we increased our investments in property and equipment for the manufacturing facility in Clearwater, Florida, and to a lesser extent, for office furniture and equipment purchases for our Brisbane, California corporate headquarters.

Net Cash Provided By Financing Activities

Net cash provided by financing activities was $147.8 million for the year ended December 31, 2016, a decrease of $87.5 million from $235.3 million for the year ended December 31, 2015. In 2015, we received aggregate net proceeds from the sale of Series B Preferred Stock and the sale of common stock in our IPO of $235.0 million. In 2016, we received net proceeds of $145.0 million from the issuance of our common stock as part of the equity investment by Nestle Health Science.

As of December 31, 2016, we had cash, cash equivalents and investments of $282.5 million, including the net proceeds we received from the issuance common stock from the Nestle Health Science equity investment of $145.0 million.

Comparison of the years ended December 31, 2015 and 2014

	Year Ended December 31,		
	2015	2014	Change
	(In thousands)		
Net cash provided by (used in):			
Operating activities	$(35,690)	$(9,777)	$(25,913)
Investing activities	(125,229)	(96)	(125,133)
Financing activities	235,327	191	235,136
Net change in cash and cash equivalents	$74,408	$(9,682)	$84,090

Net Cash Used In Operating Activities

Net cash used in operating activities was $35.7 million for the year ended December 31, 2015, an increase of $25.9 million, from $9.8 million for the year ended December 31, 2014. This increase was primarily due to higher net loss from operations resulting from increased research and development and general and administrative expenses.

Net Cash Used In Investing Activities

Cash used in investing activities of $125.2 million during the year ended December 31, 2015 consisted primarily of purchases of investments net of maturities in conjunction with the proceeds received in our IPO of $123.6 million, and certain costs associated with the manufacturing facility in Clearwater, Florida and office furniture and equipment purchases for our Brisbane, California corporate headquarters of $1.7 million. Cash used in investing activities during the year ended December 31, 2014 consisted primarily of additional investment in equipment.

Net Cash Provided By Financing Activities

Net cash provided by financing activities of $235.3 for the year ended December 31, 2015 consisted primarily of the net proceeds from the issuance of our common stock in our IPO of $168.1 million and the net proceeds from the issuance of Series B convertible preferred stock of $79.8 million, partially offset by the repurchase of shares of our Series A convertible preferred stock from certain investors of $12.9 million.

Contractual Obligations and Other Commitments

The following table summarizes our contractual obligations as of December 31, 2016:

	Years				
	Total	Less than 1	1–3	3–5	More than 5
	(In thousands)				
Operating leases [1], [2]	$10,422	$2,183	$5,702	$1,846	$691
Capital lease	161	33	102	26	—
Other purchase commitments [4]	—	—	—	—	—
Total contractual obligations	$10,583	$2,216	$5,804	$1,872	$691

[1] In June 2015, we signed a facility lease for a manufacturing facility in Clearwater, Florida. The lease calls for future aggregate lease payments of $1.7 million over a period of 10 years.

(2) In March 2015, we entered into a new lease for our corporate headquarters in Brisbane, California for 11,665 square feet of office space. Upon the commencement of the new lease in May 2015, we ceased use of our previous corporate headquarters. In August 2015, we entered into an amendment to the Brisbane, California facility lease. Pursuant to the amendment, we leased an additional 26,355 square feet of office space. The term for the new space is 72 months from the delivery of the premises to us, which took place December 2015. In addition, the term of the existing office space has been extended so that it is coterminous with the new space.

(3) In December 2016, we entered into a capital lease for equipment related to the leased facility in Florida.

(4) We purchase peanut flour, the source material for AR101, from the Golden Peanut Company pursuant to a long-term exclusive commercial supply agreement. Pursuant to the agreement, our purchase obligation commences with the first delivery of peanut flour for commercial use, which we currently anticipate will not occur prior to 2018. Assuming that our first delivery for commercial use occurs in 2018, which is not assured, the aggregate purchase commitment under this agreement would be $1.2 million over the term of five years.

We enter into agreements in the normal course of business with contract research organizations for clinical trials and with vendors for pre-clinical studies and other services and products for operating purposes which are cancelable at any time by us, generally upon 30 days prior written notice. These payments are not included in this table of contractual obligations.

Off-Balance Sheet Arrangements

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

Segment Information

We have one primary business activity and operate as one reportable segment.

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

As of December 31, 2016, we had cash, cash equivalents and investments of $282.5 million, which consisted primarily of money market funds, agency securities, corporate securities, U.S. government securities and commercial paper. Such interest-earning instruments carry a degree of interest rate risk. However, historical fluctuations of interest income have not been significant.

We do not enter into investments for trading or speculative purposes and have not used any derivative financial instruments to manage our interest rate exposure. We have not historically been exposed to material risks due to changes in interest rates. Based on our investment positions as of December 31, 2016, a hypothetical 100 basis point change in interest rates would result in a $1.0 million change in the fair market value of the portfolio. Any changes would only be realized if we sold the investments prior to maturity.

We had no outstanding debt as of December 31, 2016.

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Item 8. Financial Statements and Supplementary Data.

The following consolidated financial statements, and the related notes thereto, of Aimmune Therapeutics, Inc. and the Report of the Company's Independent Registered Public Accounting Firm are filed as a part of this Annual Report on Form 10-K.

Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders

Aimmune Therapeutics, Inc.:

We have audited the accompanying consolidated balance sheets of Aimmune Therapeutics, Inc. and subsidiaries (the Company) as of December 31, 2016 and 2015, and the related consolidated statements of operations and comprehensive loss, stockholders' equity, and cash flows for each of the years in the three year period ended December 31, 2016. 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 conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of Aimmune Therapeutics, Inc. and subsidiaries as of December 31, 2016 and 2015, and the results of their operations and their cash flows for each of the years in the three year period ended December 31, 2016, in conformity with U.S. generally accepted accounting principles.

/s/ KPMG LLP

San Francisco, California

March 15, 2017

AIMMUNE THERAPEUTICS, INC.

CONSOLIDATED BALANCE SHEETS

(In thousands, except per share amounts)

	December 31,	
	2016	2015
Assets		
Current assets:		
Cash and cash equivalents	$124,010	$76,677
Short-term investments	124,921	115,158
Prepaid expenses and other current assets	2,749	5,622
Total current assets	251,680	197,457
Long-term investments	33,602	7,992
Property and equipment, net	10,391	2,702
Prepaid expenses and other assets	3,116	4,210
Total assets	$298,789	$212,361
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$1,427	$1,863
Accrued liabilities	9,921	3,118
Other current liabilities	102	117
Total current liabilities	11,450	5,098
Other liabilities	1,367	1,012
Total liabilities	12,817	6,110
Commitments and contingencies (Note 5)		
Stockholders' equity:		
Preferred stock, par value $0.0001 per share - 10,000 shares authorized at December 31, 2016 and 2015; 0 shares issued and outstanding at December 31, 2016 and 2015	—	—
Common stock, par value $0.0001 per share—290,000 shares authorized as of December 31, 2016 and 2015; 50,204 and 42,239 shares issued and outstanding as of December 31, 2016 and 2015, respectively (including 200 and 599 shares subject to repurchase, legally issued and outstanding as of December 31, 2016 and 2015, respectively)	5	4
Additional paid-in capital	420,151	259,668
Accumulated other comprehensive loss	(27)	(88)
Accumulated deficit	(134,157)	(53,333)
Total stockholders' equity	285,972	206,251
Total liabilities and stockholders' equity	$298,789	$212,361

See accompanying notes to consolidated financial statements.

AIMMUNE THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(In thousands, except per share amounts)

	Year Ended December 31,		
	2016	2015	2014
Operating expenses			
Research and development	$54,642	$19,816	$8,181
General and administrative	26,885	16,181	2,951
Total operating expenses	81,527	35,997	11,132
Loss from operations	(81,527)	(35,997)	(11,132)
Interest income, net	703	181	12
Loss before provision for income taxes	(80,824)	(35,816)	(11,120)
Provision for income taxes	—	—	—
Net loss	(80,824)	(35,816)	(11,120)
Other comprehensive income (loss), net of tax:			
Unrealized gain (loss) on investments	61	(88)	—
Comprehensive loss	$(80,763)	$(35,904)	$(11,120)
Net loss per common share, basic and diluted	$(1.89)	$(1.88)	$(3.80)
Weighted average shares used in computing net loss per share, basic and diluted	42,751	19,041	2,929

See accompanying notes to consolidated financial statements.

AIMMUNE THERAPEUTICS, INC.

STATEMENTS OF STOCKHOLDERS' EQUITY

(In thousands)

	Series A Convertible Preferred Stock		Series B Convertible Preferred Stock		Common Stock		Additional Paid-In	Accumulated Other Comprehensive		Total Stockholders'
	Shares	Amount	Shares	Amount	Shares	Amount	Capital	Loss	Accumulated deficit	Equity
Balance as of December 31, 2013	13,264	$16,928	—	$—	2,927	$—	$1,106	$—	$(6,397)	$11,637
Issuance of common stock upon exercise of vested options	—	—	—	—	1,325	—	77	—	—	77
Stock-based compensation	—	—	—	—	—	—	77	—	—	77
Net loss	—	—	—	—	—	—	—	—	(11,120)	(11,120)
Balance as of December 31, 2014	13,264	$16,928	—	$—	4,252	$—	$1,260	$—	$(17,517)	$671
Issuance of Series B convertible preferred stock for cash at $5.69 per share, net of $221 of issuance costs	—	—	14,048	79,779	—	—	—	—	—	79,779
Issuance of common stock upon exercise of vested options	—	—	—	—	1,436	—	303	—	—	303

Issuance of common stock upon initial public offering	—	—	—	—	11,500	1	168,118	—	—	168,119
Repurchase of Series A convertible preferred stock	(2,261)	(12,874)	—	—	—	—	—	—	—	(12,874)
Conversion of preferred stock to common stock	(11,003)	(4,054)	(14,048)	(79,779)	25,051	3	83,830	—	—	—
Stock-based compensation	—	—	—	—	—	—	6,157	—	—	6,157
Other comprehensive loss	—	—	—	—	—	—	—	(88)	—	(88)
Net loss	—	—	—	—	—	—	—	—	(35,816)	(35,816)
Balance as of December 31, 2015	—	$—	—	$—	42,239	$4	$259,668	$(88)	$(53,333)	$206,251
Issuance of common stock upon exercise of vested options	—	—	—	—	413	—	2,843	—	—	2,843
Issuance of common stock upon securities purchase agreement	—	—	—	—	7,552	1	144,999	—	—	145,000
Stock-based compensation	—	—	—	—	—	—	12,641	—	—	12,641
Other comprehensive gain	—	—	—	—	—	—	—	61	—	61
Net loss	—	—	—	—	—	—	—	—	(80,824)	(80,824)
Balance as of December 31, 2016	—	$—	—	$—	50,204	$5	$420,151	$(27)	$(134,157)	$285,972

See accompanying notes to consolidated financial statements.

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AIMMUNE THERAPEUTICS, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS

(In thousands)

	Year Ended December 31,		
	2016	2015	2014
Cash flows from operating activities:			
Net loss	$(80,824)	$(35,816)	$(11,120)
Adjustments to reconcile net loss to net cash used in operating activities			
Depreciation	534	115	29
Stock-based compensation	12,641	6,157	77
Investment premium amortization, net	919	324	—
Changes in operating assets and liabilities:			
Prepaid expenses and other current assets	3,967	(9,698)	10
Accounts payable	(994)	1,072	206
Accrued liabilities	6,803	1,859	1,021
Other liabilities	340	297	—
Net cash used in operating activities	(56,614)	(35,690)	(9,777)
Cash flows from investing activities:			
Purchases of property and equipment	(7,665)	(1,708)	(56)
Purchases of investments	(197,178)	(152,811)	—
Maturities of investments	160,947	29,250	—
Change in restricted cash	—	40	(40)
Net cash used in investing activities	(43,896)	(125,229)	(96)
Cash flows from financing activities:			
Proceeds from issuance of common stock, net of issuance costs	145,000	168,119	—
Net cash proceeds from exercise of stock options, including early exercise	2,843	303	191
Proceeds from issuance of Series B convertible preferred stock, net of issuance costs	—	79,779	—
Repurchase of Series A convertible preferred stock	—	(12,874)	—
Net cash provided by financing activities	147,843	235,327	191
Net increase (decrease) in cash and cash equivalents	47,333	74,408	(9,682)
Cash and cash equivalents at the beginning of the period	76,677	2,269	11,951
Cash and cash equivalents at the end of the period	$124,010	$76,677	$2,269
Supplemental schedule of non-cash investing and financing activities:			
Purchases of property and equipment reported in accounts payable	$558	$—	$—
Conversion of convertible preferred stock	$—	$83,833	$—

to common stock at closing of initial public offering			
Capital expenditures and interest funded through long term lease obligation	$—	$710	$—
Supplemental cash flow disclosures:			
Cash paid for taxes	$—	$—	$—
Cash paid for interest	$—	$—	$—

See accompanying notes to consolidated financial statements.

AIMMUNE THERAPEUTICS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Formation and Business of the Company

Aimmune Therapeutics, Inc., or the Company, formerly known as Allergen Research Corporation, is a clinical-stage biopharmaceutical company advancing a new therapeutic approach, including the development of proprietary product candidates, for the treatment of peanut and other food allergies. Our therapeutic approach, which we refer to as Characterized Oral Desensitization Immunotherapy, or CODIT™, is a therapeutic approach designed to desensitize patients to food allergens using rigorously characterized biologic products, defined treatment protocols and tailored support services. We are headquartered in Brisbane, California and were incorporated in the state of Delaware on June 24, 2011.

Since inception, we have incurred net losses and negative cash flows from operations. During the year ended December 31, 2016, we incurred a net loss of $80.8 million and used $56.6 million of cash in operations. As of December 31, 2016, we had an accumulated deficit of $134.2 million and we do not expect to experience positive cash flows in the near future. We have financed our operations to date primarily through private placements of our equity securities and our initial public offering, or IPO, of common stock in August 2015. Our ability to continue to meet our obligations and to achieve our business objectives is dependent upon a number of factors, which include raising additional capital, obtaining U.S. Food and Drug Administration, or FDA, and European Medicines Agency, or EMA, approval and commercializing in the United States and Europe, generating sufficient revenue and our ability to continue to control expenses, if necessary, to meet our obligations as they become due for the foreseeable future. Failure to obtain FDA and EMA approval, commercialize our lead product candidate, manage discretionary expenditures or raise additional financing, as required, may adversely impact our ability to achieve our intended business objectives.

As of December 31, 2016, we had cash, cash equivalents and investments of $282.5 million. We believe that our existing capital resources will be sufficient to fund our planned operations for at least the next 12 months and through regulatory submissions for AR101, our lead investigational biologic oral immunotherapy for desensitization of patients with peanut allergy.

Private Placement

On November 23, 2016, we completed the issuance and sale of 7,522,084 shares of our common stock for an aggregate cash purchase price of $145.0 million, or the Equity Investment, pursuant to a Securities Purchase Agreement, or the Purchase Agreement, dated November 2, 2016, by and between us and Nestle Health Science US Holdings, Inc., a Delaware corporation, or Nestle Health Science. In connection with the closing of the Equity Investment, we and Nestle Health Science entered into a Standstill Agreement, or the Standstill Agreement, and a Registration Rights Agreement, or the Registration Rights Agreement. See Note 6, “Stockholders’ Equity.”

Initial Public Offering

On August 5, 2015, our registration statement on Form S-1 (File No. 333-205501) relating to the IPO of our common stock became effective. The IPO closed on August 11, 2015 at which time we issued 11,499,999 shares of our common stock at a price of $16.00 per share, which included 1,499,999 shares sold pursuant to the exercise in full of the underwriters’ option to purchase additional shares. We received proceeds of approximately $168.1 million, net of

underwriting discounts and commissions, and offering expenses. In addition, upon our IPO, all outstanding shares of convertible preferred stock converted by their terms into approximately 25.1 million shares of common stock. As of December 31, 2016, we had 50,204,383 shares of common stock outstanding. See Note 6, “Stockholders’ Equity.”

Stock Split

On July 30, 2015, we effected a 1-for-1.317 stock split of our common stock and convertible preferred stock. The par value of the authorized stock was not adjusted as a result of the stock split. In addition, we increased the number of authorized shares of common stock to 55,051,264 and the number of authorized shares of preferred stock to 25,051,264. All issued and outstanding common stock, convertible preferred stock, stock options and per share amounts contained in the accompanying consolidated financial statements and accompanying notes have been retroactively adjusted to give effect to the stock split for all periods presented. In conjunction with the our IPO, we filed our amended and restated certificate of incorporation that authorized 290,000,000 shares of common stock, $0.0001 par value per share, and 10,000,000 shares of preferred stock, $0.0001 par value per share.

2. Summary of Significant Accounting Policies

Basis of Preparation

The accompanying consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States, or U.S. GAAP, and include the accounts of our wholly-owned subsidiaries. All significant intercompany transactions have been eliminated. We operate in one reportable segment in the United States.

Foreign Currency Translation

Our functional currency and the functional currency of all of our subsidiaries is the United States dollar. Accordingly, monetary assets and liabilities in the non-functional currency of these subsidiaries are remeasured using exchange rates in effect at the end of the period. Costs in local currency are remeasured using average exchange rates for the period, except for costs related to those balance sheet items that are remeasured using historical exchange rates. The resulting remeasurement gains and losses are included in the consolidated statements of operations and comprehensive loss as incurred and have not been material for all periods presented.

Use of Estimates

The preparation of the accompanying consolidated financial statements in accordance with U.S. GAAP requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, and the reported amounts of costs and expenses during the reporting period. We base our estimates and assumptions on historical experience when available and on various factors that we believe to be reasonable under the circumstances. We evaluate our estimates and assumptions on an ongoing basis. Our actual results could differ from these estimates under different assumptions or conditions.

Cash and Cash Equivalents

We consider all highly liquid investments with original maturities of three months or less from the date of purchase to be cash equivalents. Cash equivalents, which are carried at estimated fair value, consist primarily of money market funds and certain available-for-sale investments with maturities of three months or less.

Segment Reporting

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision maker in making decisions regarding resource allocation and assessing performance. We have one operating segment.

Concentration of Credit Risk

Financial instruments that potentially subject us to a concentration of credit risk consist of cash and cash equivalents and certain investments in money market funds, agency securities, corporate securities, U.S. government securities and commercial paper. Bank deposits are primarily held by a single financial institution and these deposits may exceed insured limits. We are exposed to credit risk in the event of default by the financial institution holding our cash and cash equivalents and issuers of investments that are recorded on our consolidated balance sheets. We mitigate our risk by investing in high-grade instruments and limiting the concentration in any one issuer, which limits our exposure.

Investments

Our investments consist of available-for-sale securities. Investments with original maturities of greater than 90 days but less than one (1) year are classified as short-term on the consolidated balance sheets. Investments with original maturities greater than one (1) year are classified as long-term on the consolidated balance sheets.

Our investments in available-for-sale securities are reported at estimated fair value. Available-for-sale securities consist primarily of agency securities, corporate securities, U.S. government securities and commercial paper. Unrealized gains and losses related to changes in the fair value of securities are recognized in accumulated other comprehensive loss, net of tax, on our consolidated balance sheets. Changes in the fair value of available-for-sale securities impact the consolidated statements of operations and comprehensive loss only when such securities are sold or an other-than-temporary impairment is recognized. Realized gains and losses on the sale of securities are determined by specific identification of each security’s cost basis. We regularly review our investment portfolio to determine if any security is other-than-temporarily impaired, which would require us to record an impairment charge in the period any such determination is made. We consider factors such as the duration, severity and the reason for the decline

in value, the financial condition of the issuer and any changes thereto, the potential recovery period and our intent to sell. For debt securities, we also consider whether (i) it is more likely than not that we will be required to sell the debt securities before recovery of their amortized cost basis, and (ii) the amortized cost basis cannot be recovered as a result of credit losses. Our assessment on whether a security is other-than-temporarily impaired could change in the future due to new developments or changes in assumptions related to any particular security.

Property and Equipment

Property and equipment are stated at cost, less accumulated depreciation. Depreciation is computed using the straight-line method over the estimated useful lives of the respective assets. Maintenance and repairs are charged to the consolidated statements of operations and comprehensive loss as incurred. Upon sale or retirement of assets, the cost and related accumulated depreciation are removed from the balance sheet and the resulting gain or loss, if any, is reflected in the consolidated statements of operations and comprehensive loss.

The useful lives of property and equipment are as follows:

Furniture and office equipment	4 years
Computer equipment	3 years
Buildings	25 years
Fixtures	10 years

Impairment of Long-Lived Assets

We evaluate our 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 expected to result from the use of the asset and its eventual disposition. 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 assets. We have not recorded impairment of any long-lived assets in the periods presented.

Leases

Leases related to our corporate headquarters are classified as operating leases. Rent expense is recognized on a straight-line basis over the terms of the leases and, accordingly, we record the difference between cash rent payments and the recognition of rent expense as a deferred rent liability. Incentives granted under facilities leases are deferred and recognized as adjustments to rental expense on a straight-line basis over the term of the lease.

In June 2015, we signed a lease for a manufacturing facility in Clearwater, Florida. We were considered the deemed owner for accounting purposes. See Note 5, “Commitments and Contingencies,” for further details.

Research and Development

We expense research and development costs as incurred. We record accrued liabilities for estimated costs of research and development activities conducted by third-party service providers, which include the conduct of pre-clinical studies and clinical trials and contract manufacturing activities. These costs are a significant component of our research and development expenses. We accrue for these costs based on factors such as estimates of the work completed and in accordance with agreements established with our third-party service providers under the service agreements. We make significant judgments and estimates in determining the accrued liabilities balance in each

reporting period. As actual costs become known, we adjust our accrued liabilities. We have not experienced any material differences between accrued costs and actual costs incurred. However, the status and timing of actual services performed, number of patients enrolled and the rate of patient enrollments may vary from our estimates, resulting in adjustments to expense in future periods. Changes in these estimates that result in material changes to our accruals could materially affect our results of operations.

Stock-Based Compensation

Stock-based awards issued to employees, including stock options, are measured at fair value on the grant date using the Black-Scholes option-pricing model and recognized as expense on a straight-line basis over the employee's requisite service period (generally the vesting period). Because noncash stock compensation expense is based on awards ultimately expected to vest, it is reduced by an estimate for future forfeitures. Forfeitures are estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from estimates. There were 2,343,385, 4,192,485 and 1,635,681 stock options granted during the years ended December 31, 2016, 2015 and 2014, respectively. Additionally, there were 17,000, 0, and 0 restricted stock units awarded during the years ended December 31, 2016, 2015 and 2014 respectively.

Income Taxes

We use the asset and liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on the differences between the financial reporting and the tax bases of reported 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. We 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 our lack of earnings history, the net deferred tax assets have been fully offset by a valuation allowance.

Comprehensive Income or Loss

Comprehensive income or loss is defined as the change in equity during a period from transactions and other events, excluding changes resulting from investments from owners and distributions to owners. Other comprehensive loss includes net loss and unrealized gains and losses on available-for-sale investments.

Net Loss per Share

The following common stock equivalents were excluded from the computation of diluted net loss per share for the periods presented because their inclusion would have been antidilutive:

	Year Ended December 31,		
	2016	2015	2014
Series A convertible preferred stock	—	—	13,263,967
Stock options	5,429,267	4,814,892	2,566,559
Restricted stock units	17,000	—	—

Offering Costs

Offering costs represent underwriting, legal, accounting and other direct costs related to our IPO. These costs were deferred until completion of the IPO, at which time they were reclassified to additional paid-in capital as a reduction of the proceeds.

Fair Value Measurements

We define fair value as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market

participants on the measurement date.

Our valuation techniques are based on observable and unobservable inputs. Observable inputs reflect readily obtainable data from independent sources, while unobservable inputs reflect our market assumptions. We classify these inputs into the following hierarchy:

Level 1—Inputs are unadjusted, quoted prices in active markets for identical assets or liabilities at the measurement date;

Level 2—Inputs are observable, unadjusted quoted prices in active markets for similar assets or liabilities, unadjusted quoted prices for identical or similar assets or liabilities in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the related assets or liabilities; and

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

Financial instruments include cash equivalents, investments, accounts payable, and accrued liabilities. Our cash equivalents and investments are carried at estimated fair value and remeasured on a recurring basis. The carrying value of accounts payable and accrued liabilities approximate their estimated fair value due to the relatively short-term nature of these instruments. Our valuation techniques used to measure the fair value of money market funds were derived from quoted prices in active markets for identical assets. The valuation techniques used to measure the fair value of investments, all of which have counterparties with high credit ratings, were valued based on quoted market prices or model driven valuations using significant inputs derived from or corroborated by observable market data.

In accordance with fair value accounting requirements, companies may choose to measure eligible financial instruments and certain other items at fair value. We have not elected the fair value option for any eligible financial instruments.

Recently Issued Accounting Pronouncements Not Yet Adopted

In November 2016, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, 2016-18, Statement of Cash Flows – Restricted Cash (Topic 230), which establishes that the statement of cash flows will show the changes in cash, cash equivalents and amounts generally described as restricted cash. As a result, entities will no longer have to determine how to classify transfers to and from restricted cash within the statement of cash flows. An entity will be required to reconcile the total cash, cash equivalents and amounts generally described as restricted cash on the statement of cash flows to the amounts in the balance sheet, and disclose the nature of any restrictions on its cash, cash equivalents or amounts generally described as restricted cash. This guidance is effective for fiscal years, and interim periods within those years, beginning after December 31, 2017, and early adoption is permitted. We have not yet adopted ASU 2016-18, but we do not expect the standard to have a material impact on our consolidated financial statements and related disclosures.

In October 2016, the FASB, issued ASU, 2016-16, Income Taxes (Topic 740): Intra-Entity Transfers Other Than Inventory, which requires companies to recognize the income tax consequences of an intra-entity transfer of an asset other than inventory. This guidance will be effective for us in the first quarter of 2018, with the option to adopt it in the first quarter of 2017. We currently anticipate adopting the new standard effective January 1, 2018, and do not expect the standard to have a material impact on our consolidated financial statements and related disclosures.

In August 2016, the FASB issued ASU 2016-15, Statement of Cash Flows (Topic 230): Classification of Certain Cash Receipts and Cash Payments, which will make eight targeted changes to how cash receipts and cash payments are presented and classified in the statement of cash flows. ASU 2016-15 is effective for fiscal years beginning after December 15, 2017. ASU 2016-15 will require adoption on a retrospective basis. Early adoption is permitted. We are currently evaluating the impact that the adoption of ASU 2016-15 will have on our consolidated financial statements and related disclosures.

In June 2016, the FASB issued ASU 2016-13, Financial Instruments — Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments, which requires measurement and recognition of expected credit losses for financial assets held. ASU 2016-13 modifies the other-than-temporary impairment model for available-for-sale debt securities and requires an estimate of expected credit losses when the fair value is below the amortized cost of the asset. ASU 2016-13 is effective for fiscal years beginning after December 15, 2019 and interim periods within those fiscal years. Early adoption is permitted. We are currently evaluating the impact that the adoption of ASU 2016-13 will have on our consolidated financial statements and related disclosures.

In March 2016, the FASB, issued ASU 2016-09, Compensation—Stock Compensation (Topic 718) Improvements to Employee Share-Based Payment Accounting, which simplifies several aspects of accounting for share-based payment transactions including the income tax consequences, classification of awards as either equity or liabilities, classification on the statement of cash flows and accounting for forfeitures. The new standard is effective for fiscal years beginning after December 15, 2016, and interim periods within those fiscal years with early adoption permitted.

We do not expect the adoption of this new standard to have a material impact on our consolidated financial statements and related disclosures.

In February 2016, the FASB, issued ASU, No. 2016-02, Leases (Topic 842), which requires lessees to apply a dual approach, classifying leases as either finance or operating leases based on the principle of whether or not the lease is effectively a financed purchase by the lessee. This classification will determine whether lease expense is recognized based on an effective interest method or on a straight-line basis over the term of the lease. A lessee is also required to record a right-of-use asset and a lease liability for all leases with a term of greater than 12 months regardless of their classification. Leases with a term of 12 months or less will be accounted for similar to existing guidance for operating leases. The standard is effective for interim and annual periods beginning after December 15, 2018, with early adoption permitted. We are currently in the process of evaluating the impact the adoption of this new standard will have on our consolidated financial statements and related disclosures; however, since we are lessee to certain leases for property whose terms exceed twelve months, we expect to report assets and liabilities related to these leases on our consolidated financial statements that have not been previously reported, once we adopt ASU 2016-02.

Reclassifications

Certain amounts in the prior years have been reclassified in order to conform to the current year's presentation. None of the reclassifications impacted the results of our operations in any of the years presented.

3. Available-for-Sale Securities and Fair Value Measurements

The following table sets forth our financial instruments that were measured at fair value on a recurring basis by level within the fair value hierarchy (in thousands):

	December 31, 2016			
	Level 1	Level 2	Level 3	Total
Cash and cash equivalents:				
Cash and money market funds	$107,977	$—	$ —	$107,977
Commercial paper	—	16,033	—	16,033
Total cash and cash equivalents	$107,977	$16,033	$ —	$124,010
Investments:				
Agency securities	—	45,571	—	45,571
Corporate securities	—	22,031	—	22,031
Commercial paper	—	8,669	—	8,669
US government securities	—	82,252	—	82,252
Total investments	$—	$158,523	$ —	$158,523

	December 31, 2015			
	Level 1	Level 2	Level 3	Total
Cash and cash equivalents:				
Cash and money market funds	$61,477	$—	$ —	$61,477
Agency securities	—	9,701	—	9,701
Corporate securities	—	2,000	—	2,000
Commercial paper	—	3,499	—	3,499
Total cash and cash equivalents	$61,477	$15,200	$ —	$76,677
Investments:				
Certificates of deposit	$100	$—	$ —	$100
Agency securities	—	43,325	—	43,325
Corporate securities	—	49,596	—	49,596
Commercial paper	—	17,843	—	17,843
US government securities	—	12,286	—	12,286
Total investments	$100	$123,050	$ —	$123,150

Available-for-sale investments are carried at fair value and are included in the tables above. The aggregate market value, cost basis, and gross unrealized gains and losses of available-for-sale investments by security type, classified in cash equivalents and investments, as of December 31, 2016 are as follows (in thousands):

	December 31, 2016			
	Amortized Cost	Gross unrealized gains	Gross unrealized losses	Total fair value
Agency securities	$45,591	$ 5	$ (25)	$45,571
Corporate securities	22,050	2	(21)	22,031
Commercial paper	24,702	—	—	24,702
US government securities	82,240	15	(3)	82,252
Total available-for-sale investments	$174,583	$ 22	$ (49)	$174,556

The aggregate market value, cost basis, and gross unrealized gains and losses of available-for-sale investments by security type, classified in cash equivalents and investments, as of December 31, 2015 are as follows (in thousands):

	December 31, 2015			
	Amortized Cost	Gross unrealized gains	Gross unrealized losses	Total fair value
Agency securities	$53,062	$ 2	$ (38)	$53,026
Corporate securities	51,626	28	(58)	51,596
Commercial paper	21,342	—	—	21,342
US government securities	12,308	—	(22)	12,286
Total available-for-sale investments	$138,338	$ 30	$ (118)	$138,250

There were no gross realized gains or losses on sales of available-for-sale securities for the years ended December 31, 2016, 2015, and 2014.

Expected maturities will differ from contractual maturities because the issuers of the securities may have the right to prepay obligations without prepayment penalties.

We did not identify any other-than-temporary losses for the years ended December 31, 2016, 2015 and 2014. We do not consider unrealized losses on our other debt securities to be credit-related. These unrealized losses relate to changes in interest rates and market spreads subsequent to purchase. A substantial portion of securities that have unrealized losses are US corporate securities that are highly-rated. We have not made a decision to sell securities with unrealized losses and believe it is more likely than not we would not be required to sell such securities before recovery of its amortized cost.

4. Balance Sheet Components

Property and Equipment, Net

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

	Year Ended December 31,	
	2016	2015
Furniture and equipment	$776	$220
Computer equipment	850	324
Manufacturing equipment	703	458

Construction in progress	8,749	1,853
Property and equipment, gross	11,078	2,855
Less: accumulated depreciation	(687)	(153)
Property and equipment, net	$10,391	$2,702

Depreciation expense for the years ended December 31, 2016, 2015 and 2014 was $0.5 million, $0.1 million and $0.0 million, respectively.

Accrued Liabilities

Accrued liabilities consist of the following (in thousands):

	Year Ended December 31,	
	2016	2015
Compensation and benefits	$3,195	$1,645
Research and development	5,154	972
Professional and consulting	967	381
Other	605	120
Total accrued liabilities	$9,921	$3,118

5. Commitments and Contingencies

Facility Leases

In March 2015, we entered into a new lease for our corporate headquarters in Brisbane, California for 11,665 square feet of office space. Upon the commencement of the new lease in May 2015, we ceased use of our previous corporate headquarters. In August 2015, we entered into an amendment to the Brisbane, California facility lease. Pursuant to the amendment, we leased an additional 26,355 square feet of office space. The term for the new space is 72 months from the delivery of the premises to us, which took place December 2015. In addition, the term of the existing office space has been extended so that it is coterminous with the new space. The amendment required a total security deposit of approximately $0.3 million. We are responsible for operating expenses over base operating expenses as defined in the headquarters lease agreement.

In June 2015, we signed a facility lease for a manufacturing facility for approximately 20,000 square feet of manufacturing space in Clearwater, Florida. The initial term of the lease is for 120 months. For accounting purposes, due to the nature and extent of our involvement with the construction of this manufacturing facility, we were considered to be the owner of the assets during the construction period through the lease commencement date, even though the lessor is responsible for funding and repairing components of the building shell and constructing a portion of the related building infrastructure. Construction to this building commenced in July 2015 and as of December 31, 2016, we have incurred approximately $0.3 million of construction and equipment costs related to the building, which is recorded in construction in progress. We also recorded $0.7 million to construction in progress for costs incurred by the lessor and recognized a corresponding amount included within other liabilities within the consolidated balance sheet. We are responsible for operating expenses including real estate taxes as defined in the manufacturing facility lease agreement.

Total future aggregate minimum lease payments under our operating leases are as follows (in thousands):

Year Ended December 31,	
2017	$2,216
2018	1,919
2019	1,905
2020	1,980
2021	1,872
and after	691
Total	$10,583

Rent expense under operating leases for the years ended December 31, 2016, 2015 and 2014 was $1.7 million, $0.6 million and $0.1 million, respectively.

Capital Lease

In July 2016, we entered into a five year capital lease agreement for certain equipment in our Florida manufacturing facility. The current portion of the capital lease obligation is included in Other Current Liabilities and the noncurrent portion is included in Other Liabilities.

The following is a schedule of future minimum lease payments due under the capital lease obligation as of December 31, 2016 (in thousands):

Year Ended December 31,	
2017	$33
2018	33
2019	34
2020	35
2021	26
Total capital lease obligation	161
Less: amount representing interest	64
Present value of net minimum capital lease payments	97
Less: current portion	12
Total noncurrent capital lease obligation	$85

Purchase Commitments

We purchase peanut flour, the source material for AR101, from the Golden Peanut Company pursuant to a long term exclusive commercial supply agreement. Pursuant to the agreement, our purchase obligation commences with the first delivery of peanut flour for commercial use, which we currently anticipate will not occur prior to 2018. Assuming that our first delivery for commercial use occurs in 2018, which is not assured, the aggregate purchase commitment under this agreement would be $1.2 million over a term of five years.

Indemnifications

We indemnify each of our officers and directors for certain events or occurrences, subject to certain limits, while the officer or director is or was serving at the Company's request in such capacity, as permitted under Delaware law and in accordance with our certificate of incorporation and bylaws. The term of the indemnification period lasts as long as an officer or a director may be subject to any proceeding arising out of acts or omissions of such officer or director in such capacity. The maximum amount of potential future indemnification is unlimited; however, we currently hold directors and officers liability insurance. This insurance allows the transfer of risk associated with our exposure and may enable us to recover a portion of any future amounts paid. We believe that the fair value of these indemnification obligations is minimal. Accordingly, we have not recognized any liabilities relating to these obligations for any period.

Legal

During the normal course of business, we may be a party to legal claims that may not be covered by insurance. We do not believe that any such claims would have a material impact on our consolidated financial statements.

6. Stockholders' Equity

Convertible Preferred Stock

In January and February 2015, we issued an aggregate 14,047,996 shares of Series B convertible preferred stock, $0.0001 par value, original issue price of $5.69 per share, for gross cash proceeds of $80.0 million, and in January 2015, we repurchased 2,260,706 shares of Series A convertible preferred stock from certain investors. The purchase price of the Series A convertible preferred stock was $5.69 per share, the same as the issue price of the Series B convertible stock, and was at an aggregate cost of $12.9 million. The offering costs for the issuance and sale of Series B convertible preferred stock was $221,000. All 25,051,257 shares of our then-outstanding convertible preferred stock converted into an equivalent number of shares of common stock upon the closing of our IPO on August 11, 2015.

As of December 31, 2016 and 2015, we had authorized 10,000,000 shares of convertible preferred stock, and no shares of convertible preferred stock were issued and outstanding.

Common Stock

On November 23, 2016, we issued and sold 7,522,084 shares of our common stock, par value $0.0001 per share, for an aggregate cash purchase price of $145.0 million, pursuant to the Purchase Agreement, dated November 2, 2016, by and between us and Nestle Health Science. In connection with the closing of the Equity Investment, we and Nestle Health Science entered into a Registration Rights Agreement and a Standstill Agreement.

Under the terms of the Registration Rights Agreement, upon the written request of Nestle Health Science, we shall prepare and file with the Securities and Exchange Commission, or the Commission, a registration statement covering the resale of all the shares sold to Nestle Health Science that are not then registered on an existing and effective registration statement for an offering to be made on a continuous basis pursuant Commission Rule 415. Additionally,

we shall use commercially reasonable efforts to cause such registration statement filed under the Registration Rights Agreement to be declared effective under the Securities Act of 1933, as amended, within certain defined time limits and to keep such registration statement continuously effective for a period of potentially three years from the original effect date of such registration statement.

Under the terms of the Standstill Agreement, Nestle Health Science is prohibited from entering into transactions with the shares purchased in the Equity Investment, as well as to enter into any transactions with any of our assets, without prior written consent of a majority of the members of our board of directors until the later of the end of the term of the Collaboration Agreement and November 23, 2018.

7. Stock-Based Awards

Equity Plans

In July 2015, we adopted the 2015 Stock Plan, or the 2015 Plan. Under the 2015 Plan, 4,681,544 shares of our common stock were initially reserved for the issuance of stock options and restricted stock to employees, directors, and consultants under terms and provisions established by the Board of Directors, or the Board, and approved by our stockholders. As of December 31, 2016 and December 31, 2015 there were 4,344,487 and 4,443,479 and shares available for future grant, respectively.

Under the terms of the 2015 Plan, options may be granted at an exercise price not less than fair market value. For employees holding more than 10% of the voting rights of all classes of stock, the exercise prices for incentive stock options may not be less than 110% of fair market value, as determined by the Board. The terms of options granted under the 2015 Plan may not exceed ten years. All options issued to date have had a ten-year life. To date, options granted generally vest in three ways: 1) over four years at a rate of 25% upon the first anniversary of the issuance date and 1/48th per month thereafter, 2) over two years at a rate of 1/24th per month, or 3) over four years at a rate of 1/48th per month. The 2015 Plan contains certain change of control provisions and the employment offer letters of certain employees provide for varied acceleration of vesting in the event of a change of control and/or termination without cause. It also contains a net exercise provision and allows for cashless exercise upon the class of shares subject to the option becoming publicly traded in an established securities market.

Our 2013 Stock Plan, or the 2013 Plan, which was originally adopted during January 2013, was terminated upon consummation of our IPO in August 2015. As a terminated plan, no further options can be granted from the 2013 Plan, and no further shares are reserved for issuance under the 2013 Plan.

Prior to its termination, the 2013 Plan allowed employees to exercise a stock option in exchange for cash before the requisite service is provided (e.g., before the award is vested under its original terms); however, such arrangements permit us to subsequently repurchase such shares at the exercise price if the vesting conditions are not satisfied. Such an exercise is not substantive for accounting purposes. Therefore, the payment received by us for the exercise price is recognized as an early exercise liability on the consolidated balance sheets and will be transferred to common stock and additional paid-in capital as such shares vest. As of December 31, 2016 and December 31, 2015, 199,538 and 599,242 unvested shares were legally issued and outstanding, respectively. In connection with these unvested shares, we have recorded an early exercise liability as of December 31, 2016 and 2015 of $0.06 million and $0.22 million, respectively, of which $0.05 million and $0.14 million is included in other current liabilities as of December 31, 2016 and 2015, respectively, and $0.01 million $0.08 million is included in other liabilities as of December 31, 2016 and 2015, respectively, in the consolidated balance sheets. These shares are excluded from basic and diluted net loss per share until our repurchase right lapses and the shares are no longer subject to the repurchase feature.

Activity under the 2015 Plan and 2013 Plan is set forth below:

	Options Outstanding		
	Number of Options and Unvested Shares	Weighted-Average Exercise Price	Weighted Average Remaining Contractual Life	Aggregate Intrinsic Value (in

			(in years)	thousands)
Balance, December 31, 2015	4,814,892	$ 5.20	9.23	$ 64,211
Options granted	2,343,385	$ 16.02		
Options exercised and shares vested	(813,102)	$ 3.49		
Options repurchased	(68,150)	$ 0.14		
Options cancelled	(648,118)	$ 9.64		
Balance, December 31, 2016	5,628,907	$ 9.50	9.02	$ 61,617
Options vested and expected to vest as of December 31, 2016	5,422,307	$ 9.41	8.68	$ 59,856
Options exercisable as of December 31, 2016	3,344,876	$ 2.96	8.66	$ 51,749

The aggregate intrinsic values of options outstanding, exercisable, and vested and expected to vest were calculated as the difference between the exercise price of the options and the market price for shares of our common stock as of December 31, 2016. The 2013 Plan provided for early exercise, therefore, all the Company’s outstanding stock options issued under that plan are exercisable. The total intrinsic value of options exercised during the year ended December 31, 2016 was $6.5 million.

Stock Options Granted

Stock options granted during the years ended December 31, 2016, 2015, and 2014 had a per share weighted-average grant-date fair value of $10.53, $6.11 and $0.09, respectively. The fair value is being expensed over the vesting period of the options, which is either four years or two years on a straight-line basis as the services are being provided. No tax benefits were realized from options during the periods. We issued one grant totaling 213,354 options to a non-employee during the year ended December 31, 2015. The fair value of the non-employee options was measured using the Black-Scholes option-pricing model reflecting the same assumptions as applied to employee options, other than the expected life, which was assumed to be the remaining contractual life of the option. During 2016, we converted the non-employee to an employee, and converted the grant from a non-employee grant to an employee grant. The conversion of the grant was treated as a modification of the original grant; accordingly, we recognized $0.09 million of modification expense.

As of December 31, 2016 and 2015, total unrecognized stock-based compensation expense was $27.3 million and $17.2 million, which is expected to be recognized over the weighted-average remaining vesting period of 2.72 years and 3.23 years, respectively.

Restricted stock unit, or RSU, activity under the 2015 Plan is set forth below:

	Shares	Weighted Average Grant Date Fair Value
Unvested Balance, December 31, 2015	—	$ —
Awarded	17,000	14.01
Released	—	—
Forfeited	—	—
Unvested Balance, December 31, 2016	17,000	$ 14.01

RSUs are measured based on the fair market value of the underlying stock on the date of grant and recognized as expense on a straight-line basis over the employee’s requisite service period (generally the vesting period). As of December 31, 2016, there was $0.1 million of unrecognized compensation expense related to RSUs, which is expected to be recognized over a weighted-average period of 0.2 years.

Determining Fair Value of Stock Options

Prior to our IPO, the fair value of our shares of common stock underlying the stock options was the responsibility of and determined by our Board. Because there was no public market for our common stock, the Board determined the fair value of common stock at the time of grant of the option by considering a number of objective and subjective factors, including independent third-party valuations of our common stock, sales of convertible preferred stock to unrelated third parties, operating and financial performance, the lack of liquidity of capital stock and general and industry specific economic outlook, amongst other factors. Following the IPO, the market traded price of the shares of common stock underlying the stock options is the closing price of our stock as reported on The NASDAQ Global Select Market on the grant date.

In determining the fair value of the stock-based awards used to calculate stock-based compensation expense, we use the Black-Scholes option-pricing model and assumptions discussed below. Each of these inputs is subjective and

generally requires significant judgment to determine.

- Expected Term. The expected term of stock options represents the weighted average period the stock options are expected to be outstanding. We have opted to use the simplified method for estimating the expected term as provided by the Securities and Exchange Commission Staff Accounting Bulletin, SAB, 110 as our options grants are considered “plain vanilla”. The simplified method calculates the expected term as the average time- to-vesting and the contractual life of the options. We plan to continue to use the simplified method under SAB 110 until we have sufficient exercise history as a publicly traded company.
- Expected Volatility. The expected stock price volatility assumption was determined by examining the historical volatilities of a group of industry peers, as we have limited trading history for our common stock. Industry peers consist of several public companies in the biopharmaceutical industry with comparable characteristics including enterprise value, risk profiles and position within the industry. We intend to continue to consistently apply this process using the same or similar public companies until a sufficient amount of historical information regarding the volatility of our own common stock share price becomes available, or unless circumstances change such that the identified companies are no longer similar to us, in which case, more suitable companies whose share prices are publicly available would be utilized in the calculation.

- Risk-Free Interest Rate. The risk-free interest rate is based on the Black-Scholes valuation model on the implied yield available on U.S. Treasury zero-coupon issues in effect at the time of grant for periods corresponding with the expected term of the option.

Expected Dividend Yield. We have never paid dividends on our common stock and have no plans to pay dividends on our common stock. Therefore, we used an expected dividend yield of zero.

The following table presents the weighted-average assumptions used to estimate the fair value of options granted:

	Year Ended December 31,		
	2016	2015	2014
Expected volatility	74.46%	74.14%	79.62%
Risk-free interest rate	1.71 %	1.73 %	1.51 %
Expected dividend yield	—	—	—
Expected term (in years)	6.03	5.99	4.65
Weighted average grant date fair value	$10.53	$6.11	$0.09

Stock-based compensation expense, net of estimated forfeitures, is reflected in the statements of operations and comprehensive loss (in thousands) as summarized below:

	Year Ended December 31,		
	2016	2015	2014
Research and development	$4,838	$2,522	$ 23
General and administrative	7,803	3,635	54
Total stock-based compensation expense	$12,641	$6,157	$ 77

During the years ended December 31, 2016, 2015 and 2014, we recorded $0.9 million, $1.4 million and $0 of stock compensation expense related to the acceleration of certain former executives' stock options, respectively.

8. Income Taxes

We did not record a tax provision for the years ended December 31, 2016, 2015 and 2014 as we incurred net losses in each period, and the need for a full valuation allowance on deferred tax assets.

The following table presents loss before provision for income taxes (in thousands):

	Year Ended December 31,		
	2016	2015	2014
Income/(loss) before income taxes			

Domestic	$(66,210)	$(17,489)	$(11,120)
Foreign	(14,614)	(18,327)	—
Total loss before provision for income taxes	$(80,824)	$(35,816)	$(11,120)

Income tax expense for the years ended December 31, 2016, 2015 and 2014 differed from the amount expected by applying the statutory federal tax rate to the loss before taxes as summarized below (in thousands):

	Year Ended December 31,		
	2016	2015	2014
Federal tax benefit at statutory rate	34.00 %	34.00 %	34.00 %
State tax benefit, net of federal benefit	0.39 %	3.02 %	6.33 %
Stock compensation	-1.75 %	-1.59 %	0.00 %
Change in valuation allowance	-27.45%	-20.55%	-41.23%
Research and development credits	2.53 %	2.52 %	1.08 %
Foreign income taxed at different rates	-6.13 %	-17.40%	0.00 %
Other	-1.59 %	0.00 %	-0.18 %
Income tax expense	0.00 %	0.00 %	0.00 %

The significant components of our deferred taxes are as follows (in thousands):

	Year Ended December 31,	
	2016	2015
Deferred tax assets (liabilities):		
Net operating loss carryforwards	$27,109	$9,857
Start-up costs	1,282	1,612
Stock-based compensation	3,427	1,413
Tax credit carryforwards	3,585	1,296
Accruals	1,041	195
Other	22	(2)
Total deferred tax assets	36,466	14,371
Less: valuation allowance	(36,466)	(14,371)
Net deferred income taxes	$—	$—

We recognize deferred income taxes for temporary differences between the basis of assets and liabilities for financial statement and income tax purposes. We periodically evaluate the positive and negative evidence bearing upon realizability of our deferred tax assets. Based upon the weight of available evidence, which includes our historical operating performance, reported cumulative net losses since inception and difficulty in accurately forecasting our future results, we maintained a full valuation allowance on the net deferred tax assets as of December 31, 2016 and 2015. We intend to maintain a full valuation allowance on the federal and state deferred tax assets until sufficient positive evidence exists to support reversal of the valuation allowance. The net change in the valuation allowance for the years ended December 31, 2016 and December 31, 2015 was an increase of $22.1 million and $7.4 million, respectively.

As of December 31, 2016, we had net operating loss, or NOL, carryforwards for Federal, California and other state income tax purposes of $81.0 million, $12.0 million, and $2.4 million, respectively. As of December 31, 2015, we had NOL carryforwards for Federal, California and other state income tax purposes of $24.7 million, $12.0 million, and $0.4 million, respectively, which will begin to expire in 2031, 2031, and 2030, respectively, if not utilized. $3.6 million, $0.0 million, and $0.1 million of the Federal, California, and other state NOL carryforwards, respectively, relates to windfall stock option deductions, which, when we adopt ASU 2016-09, will increase our NOL carryforwards deferred tax assets and our valuation allowance.

At December 31, 2016 and 2015, we had Federal and California research credit carryforwards of $3.9 million and $0.9 million, respectively. The Federal research credits will begin to expire in 2032, while the California research credits have no expiration date.

Our ability to utilize NOL carryforwards or other tax attributes, such as research tax credits, in any taxable year may be limited if we have experienced an ownership change under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code. Following issuance of the Series B convertible preferred stock in January and February 2015, we performed a preliminary Section 382 analysis and believe that we experienced multiple ownership changes prior to June 30, 2015, and, as a result, such federal and state NOL carryforwards and our tax credits are subject to limitation. We have not performed a Section 382 analysis to evaluate whether or not we experienced an ownership change as a result of either our August 2015 IPO or the November 2016 Equity Investment by Nestle Health Science.

Tax benefits from uncertain tax positions are recognized when it is more likely than not that the position will be sustained upon examination, including resolutions of any related appeals or litigation processes, based on technical

merits. The amount recognized is measured as the largest amount of tax benefit that is greater than 50% likely of being realized upon effective settlement.

The following table summarizes the activity related to our unrecognized benefits (in thousands):

	Year Ended December 31,	
	2016	2015
Beginning balance - unrecognized tax benefit, gross	$ —	$ —
Increases related to tax positions taken during a prior year	—	—
Decreases related to a tax position taken during a prior year	—	—
Increases related to tax positions taken during the current year	960	—
Decreases related to settlements with taxing authorities	—	—
Decreases related to expiration of statute of limitations	—	—
Ending balance - unrecognized tax benefits, gross	$ 960	$ —

At December 31, 2016, the unrecognized tax benefits for uncertain tax positions were offset against the deferred tax assets and would not affect the income tax rate if recognized due to our being in a valuation allowance position. Our policy is to include interest and penalties related to unrecognized tax benefits, if any, within the provision for taxes in the consolidated statements of operations. We did not accrue any interest or penalties for the years ended December 31, 2016 and 2015. We do not have any tax positions for which it is reasonably possible that the total amount of gross unrecognized tax benefits will significantly change within 12 months of December 31, 2016.

We file federal, state and foreign income tax returns in jurisdictions with varying statutes of limitations. Due to our NOL carryforwards, our income tax returns remain subject to examination by federal and most state taxing authorities for all tax years.

9. Defined Contribution Plan

We sponsor a 401(k) Plan, or the 401(k) Plan, which stipulates that eligible employees may contribute to the 401(k) Plan subject to certain limitations. We may match employee contributions in amounts to be determined at our sole discretion. To date, we have not made any matching contributions.

10. Selected Quarterly Results of Operations (Unaudited)

The following table presents our unaudited quarterly financial data. Our quarterly results of operations for these periods are not necessarily indicative of our future results of operations.

	Quarter Ended			
	March 31	June 30	September 30	December 31
2016	(In thousands, except per share data)			
Operating expenses:				
Research and development	$9,976	$11,820	$15,888	$16,958
General and administrative	5,723	6,466	6,353	8,343
Total operating expenses	15,699	18,286	22,241	25,301
Loss from operations	(15,699)	(18,286)	(22,241)	(25,301)
Interest income, net	176	147	155	225
Net loss	$(15,523)	$(18,139)	$(22,086)	$(25,076)
Net loss per common share, basic and diluted	$(0.37)	$(0.43)	$(0.53)	$(0.55)

	Quarter Ended			
	March 31	June 30	September 30	December 31
2015	(In thousands, except per share data)			
Operating expenses:				
Research and development	$2,069	$3,131	$3,850	$10,766
General and administrative	1,372	4,246	5,174	5,389
Total operating expenses	3,441	7,377	9,024	16,155
Loss from operations	(3,441)	(7,377)	(9,024)	(16,155)
Interest income, net	—	1	33	147
Net loss	$(3,441)	$(7,376)	$(8,991)	$(16,008)
Net loss per common share, basic and diluted	$(0.81)	$(1.60)	$(0.36)	$(0.39)

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

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures.

As required by Rule 13a-15(b) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, our management, under the supervision and with the participation of our Chief Executive Officer and Chief Financial Officer, has evaluated the effectiveness of the design and operation of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of December 31, 2016. Based on the evaluation of our disclosure controls and procedures, our Chief Executive Officer and Chief Financial Officer have concluded that, as of December 31, 2016, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting (as defined in Rule 13a-15(f) and 15d-15(f) of the Exchange Act). Internal control over financial reporting is a process designed by, or under the supervision of, our Chief Executive Officer and Chief Financial Officer, and effected by our Board of Directors, management and other personnel, 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 and includes those policies and procedures that:

- Pertain to the maintenance of records that accurately and fairly reflect in reasonable detail the transactions and dispositions of the assets of our company;

- Provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors; and

- Provide reasonable assurances regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material adverse effect on our financial statements.

Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting as of December 31, 2016 based on the criteria established in Internal Control - Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission, or COSO 2013. Based on our evaluation under the criteria set forth in Internal Control - Integrated Framework issued by the COSO, our management concluded our internal control over financial reporting was effective as of December 31, 2016.

Attestation Report of the Registered Public Accounting Firm

This Annual Report on Form 10-K does not include an attestation report of our registered public accounting firm due to an exemption established by the JOBS Act for "emerging growth companies."

Changes in Internal Control over Financial Reporting.

There were no changes in our internal control over financial reporting during the quarter ended December 31, 2016 identified in connection with the evaluation required by Rule 13a-15(d) and 15d-15(d) of the Exchange Act that have

materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Inherent Limitations on Effectiveness of Controls

Internal control over financial reporting may not prevent or detect all errors and all fraud. A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Also, projections of any evaluation of effectiveness of internal control to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate. Accordingly, our disclosure controls and procedures are designed to provide reasonable, not absolute, assurance that the objectives of our disclosure control system are met.

Item 9B. Other Information.

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

Information required by this Item is incorporated herein by reference to the sections titled “Executive Officers,” “Election of Directors,” “Corporate Governance” and “Section 16(a) Beneficial Ownership and Reporting Compliance” in our Definitive Proxy Statement with respect to our 2017 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

Item 11. Executive Compensation.

Information required by this Item is incorporated herein by reference to the section titled “Executive Compensation,” “Director Compensation” and “Corporate Governance” in our Definitive Proxy Statement with respect to our 2017 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

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

Information required by this Item is incorporated herein by reference to the section titled “Security Ownership of Certain Beneficial Owners and Management” and “Equity Compensation Plan Information” in our Definitive Proxy Statement with respect to our 2017 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

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

Information required by this Item is incorporated herein by reference to the section titled “Certain Relationships and Related Party Transactions” and “Corporate Governance” in our Definitive Proxy Statement with respect to our 2017 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

Item 14. Principal Accounting Fees and Services.

Information required by this Item is incorporated herein by reference to the section titled “Ratification of Selection of Independent Registered Public Accounting Firm” in our Definitive Proxy Statement with respect to our 2017 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(a) The following documents are filed as part of this Annual Report on Form 10-K:

1. Financial Statements

See Index to Financial Statements at Item 8 herein.

2. Financial Statement Schedules

All schedules are omitted because they are not applicable or the required information is shown in the financial statements or notes thereto.

3. Exhibits

See the Exhibit Index immediately following the signature page of this Annual Report on Form 10-K.

Item 16. Form 10-K Summary.

Registrants may voluntarily include a summary of information required by Form 10-K under Item 16. We have elected not to include such summary.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Annual Report on Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized.

Aimmune Therapeutics, Inc.

Date: March 15, 2017 By: /s/ Stephen G. Dilly
Stephen G. Dilly, M.B.B.S., PhD.
President, Chief Executive Officer and Director

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints each of Stephen G. Dilly, M.B.B.S., PhD. and Douglas T. Sheehy his or her true and lawful attorney-in-fact and agent, with full power of substitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorney-in-fact and agent, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorney-in-fact and agent, or his substitutes or substitute, may lawfully do or cause to be done by virtue hereof.

IN WITNESS WHEREOF, each of the undersigned has executed this Power of Attorney as of the date indicated opposite his/her name.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Annual Report on Form 10-K has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ Stephen G. Dilly Stephen G. Dilly	President, Chief Executive Officer and Director (Principal Executive Officer)	March 15, 2017
/s/ Warren L. DeSouza Warren L. DeSouza	Chief Financial Officer (Principal Financial and Accounting Officer)	March 15, 2017
/s/ Gregory Behar	Director	March 15, 2017

Gregory Behar		
/s/ Patrick G. Enright Patrick G. Enright	Director	March 15, 2017
/s/ Kathryn E. Falberg Kathryn E. Falberg	Director	March 15, 2017
/s/ Mark T. Iwicki Mark T. Iwicki	Director	March 15, 2017
/s/ Mark D. McDade Mark D. McDade	Director	March 15, 2017
/s/ Stacey D. Seltzer Stacey D. Seltzer	Director	March 15, 2017

Exhibit Index

Exhibit Number	Exhibit Description	Incorporated by Reference Form	Date	Number	Filed Herewith
3.1	Amended and Restated Certificate of Incorporation of Aimmune Therapeutics, Inc.	8-K	8/11/2015	3.1	
3.2	Amended and Restated Bylaws of Aimmune Therapeutics, Inc.	8-K	8/11/2015	3.2	
4.1	Reference is made to exhibits 3.1 through 3.2.				
4.2	Form of Common Stock Certificate.	S-1/A	7/27/2015	4.2	
4.3	Amended and Restated Investors' Rights Agreement, dated January 20, 2015, by and among Aimmune Therapeutics, Inc. and the investors listed therein.	S-1	7/6/2015	10.1	
4.4	Registration Rights Agreement, dated November 23, 2016, by and between the Company and Nestle Health Science US Holdings, Inc.				X
4.5	Standstill Agreement, dated November 23, 2016, by and between the Company and Nestle Health Science US Holdings, Inc.				X
10.1†	Supply Agreement, dated as of October 13, 2014, by and between the Company and Golden Peanut Company, L.L.C.	S-1	7/6/2015	10.2	
10.2(a)	Office Lease, dated February 23, 2015, by and between, the Company, Diamond Marina LLC and Diamond Marina II LLC.	S-1	7/6/2015	10.3	
10.3(b)	First Amendment to Office Lease, dated August 26, 2015, by and between, the Company, Diamond Marina LLC and Diamond Marina II LLC.	10-Q	8/31/2015	10.2	
10.4(a)†	Manufacturing Facility Lease, dated June 8, 2015, by and between, the Company and MIDA Group, LLC.	S-1	7/6/2015	10.4	
10.4(b)	Amendment to Manufacturing Facility Lease, dated June 8, 2016, by and between the Company and Myerlake, LLC.	10-Q	8/10/2016	10.2	
10.5(a)††	Strategic Collaboration Agreement, dated November 3, 2016, by and between the Company and Nestec Ltd.				X
10.5(b)	Securities Purchase Agreement, dated November 3, 2016, by and between the Company and Nestle Health Science US Holdings, Inc.				X

10.6(a)#	2013 Stock Plan.	S-1	7/6/2015	10.5(a)
10.6(b)#	Amendment to the 2013 Stock Plan, dated January 20, 2015.	S-1	7/6/2015	10.5(b)
10.6(c)#	Form of Stock Option Grant Notice and Stock Option Agreement under the 2013 Stock Plan.	S-1	7/6/2015	10.5(c)
10.6(d)#	Form of Restricted Stock Purchase Grant Notice and Restricted Stock Purchase Agreement under the 2013 Stock Plan.	S-1	7/6/2015	10.5(d)
10.7(a)#	2015 Equity Incentive Annual Plan.	S-8	8/1/2015	99.2(a)
10.7(b)#	Form of Stock Option Grant Notice and Stock Option Agreement under the 2015 Equity Incentive Annual Plan.	S-1/A	7/27/2015	10.6(b)
10.7(c)#	Form of Restricted Stock Award Agreement and Restricted Stock Unit Award Grant Notice under the 2015 Equity Incentive Annual Plan.	S-1/A	7/27/2015	10.6(c)
10.8#	Form of Indemnification Agreement for directors and officers.	S-1/A	7/27/2015	10.7

Exhibit		Incorporated by Reference			Filed
Number	Exhibit Description	Form	Date	Number	Herewith
10.9#	Executive Employment Agreement, dated July 24, 2015, by and between the Company and Stephen G. Dilly, M.B.B.S., Ph.D.	S-1/A	7/27/2015	10.8	
10.10#	Executive Employment Agreement, dated July 24, 2015, by and between the Company and Mary M. Rozenman.	S-1/A	7/27/2015	10.12	
10.11#	Aimmune Therapeutics UK Ltd. UK Employment Agreement for Sue Barrowcliffe, dated February 19, 2016, by and between the Company and Susan E. Barrowcliffe.	10-K	3/3/2016	10.14	
10.12#	Offer Letter, dated November 20, 2015, by and between the Company and Jeffrey Knapp.	10-K	3/3/2016	10.15	
10.13#	Executive Employment Agreement, effective February 1, 2016, by and between the Company and Jeffrey H. Knapp.	10-Q	5/16/2016	10.2	
10.14#	Executive Employment Agreement, dated April 4, 2016, by and between the Company and Douglas T. Sheehy.	10-Q	5/16/2016	10.3	
10.15#	Executive Employment Agreement, dated June 16, 2016, by and between the Company and Daniel Adelman.	10-Q	8/10/2016	10.3	
10.16#	Executive Employment Agreement, dated July 24, 2015, by and between the Company and Warren L. DeSouza	S-1/A	7/27/2015	10.9	
10.17#	Transition and Separation Agreement, dated February 3, 2017, by and between the Company and Warren L. DeSouza.	8-K	2/3/2017	10.1	
10.18#	Executive Employment Agreement, dated July 24, 2015, by and between the Company and Robert M. Elfont.	S-1/A	7/27/2015	10.11	
10.19#	Separation Agreement, dated July 13, 2016, by and between the Company and Robert Elfont.	10-Q	8/10/2016	10.4	
10.20#	Aimmune Therapeutics, Inc. Employee Stock Purchase Plan.	S-8	7/27/2015	99.3	
10.21#	Non-Employee Director Compensation Program.	S-1/A	7/27/2015	10.16	
10.22#	Aimmune Therapeutics, Inc. Corporate Bonus Plan.	8-K	2/25/2016	10.1	
21.1	List of subsidiaries	S-1/A	7/27/2015	21.1	
23.1	Consent of independent registered public accounting firm.				X
24.1	Power of Attorney. Reference is made to the signature page to the Registration Statement.				X

31.1	Certification of Principal Executive Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	X
31.2	Certification of Principal Financial Officer Pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as Adopted Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.	X
32.1**	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	X
32.2**	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	X
101.INS	XBRL Instance Document	X

Exhibit Number	Exhibit Description	Incorporated by Reference Form	Date	Number	Filed Herewith
101.SCH	XBRL Taxonomy Extension Schema Document				X
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document				X
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document				X
101.LAB	XBRL Taxonomy Extension Label Linkbase Document				X
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document				X

† Confidential treatment has been granted for certain information contained in this exhibit. Such information has been omitted and filed separately with the Securities and Exchange Commission.

†† Portions of this exhibit (indicated by asterisks) have been omitted pursuant to a request for confidential treatment filed separately with the Securities and Exchange Commission.

# Indicates management contract or compensatory plan.

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